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The Manitoba Cancer Treatment and Research Foundation

Annual Report for the Year 1985

OUR COVER

Jeffrey, our teaching puppet in conversation with a patient. Jeffrey, who has veins, tears, and internal organs is used to explain treatment to these children.

1985 ANNUAL REPORT

Edited by: J. Singer, Manitoba Cancer Foundation

Cover Design and Publication: Printing Group, Communication Systems, The University of Manitoba.

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W. L. Milne, Esq.,
Chairman
The Manitoba Cancer Treatment
and Research Foundation

Sir:

It is my pleasure to submit to you the Annual Report of the Manitoba Cancer Treatment and Research Foundation. The body of the report documents the activities of patient care, support services, educational programs and research for 1985. A supplement to the body of the report includes the cancer incidence and mortality figures for the Province for that year. Not documented are the major efforts of the Foundation and its staff to upgrade outpatient services, radiotherapy facilities and the provision of dedicated oncology beds and inpatient services. These issues remained unresolved at the close of 1985.

Again it is my sincere pleasure to acknowledge the support of a staff whose dedication makes possible the work and the purpose of the Foundation.

Respectfully submitted,

L. G. Israels, M.D.
Executive Director

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

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Assistant Executive Director — R. R. Publow
Executive Secretary — J. Singer
Administrative Assistant Finance — I. Birse
Administrative Assistant Personnel — J. Morton
Accounts Payable — M. Nash

PROFESSIONAL STAFF

The Foundation is an integral part of the teaching and research program of the University of Manitoba. Various staff members participate in the undergraduate oncology program, teach on the hospital wards, and have graduate students in their laboratories.

UNIVERSITY APPOINTMENTS

Faculty of Medicine

Department of Anatomy
Dr. G. Froese, *Associate Professor*

Department of Biochemistry
Dr. J. Wright, *Professor*
Dr. L. G. Israels, *Adjunct Professor*

Department of Immunology
Dr. F. Paraskevas, *Professor*
Dr. A. Greenberg, *Associate Professor*
Dr. D. A. Chow, *Assistant Professor*

Department of Internal Medicine
Dr. G. J. Goldenberg, *Professor*
Dr. L. G. Israels, *Distinguished Professor*
Dr. F. Paraskevas, *Professor*
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Dr. B. Weinerman, *Associate Professor*
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Dr. E. Bow, *Assistant Professor*
Dr. L. Brandes, *Assistant Professor*
Dr. H. Y. P. Lam, *Assistant Professor*
Dr. S. T. Lee, *Assistant Professor*
Dr. H. Schipper, *Assistant Professor*
Dr. J. Wright, *Adjunct Professor*

Department of Microbiology
Dr. J. Wright, *Professor*

Department of Obstetrics and Gynaecology
Dr. G. V. Krepart, *Associate Professor*
Dr. R. J. Lotocki, *Assistant Professor*

Department of Pediatrics
- Dr. A. Bishop, *Professor*
- Dr. A. H. Greenberg, *Associate Professor*
- Dr. J. M. Gerrard, *Associate Professor*
- Dr. E. D. Israels, *Associate Professor*
- Dr. M. Schroeder, *Associate Professor*
- Dr. S. J. Israels, *Assistant Professor*
- Dr. N. Kobrinsky, *Assistant Professor*

Department of Physiology
- Dr. J. Dodd, *Assistant Professor*
- Dr. M. Mowatt, *Assistant Professor*

Department of Radiology
- Dr. J. M. Gillies, *Associate Professor*
- Dr. K. Malaker, *Associate Professor*
- Dr. S. Shalev, *Associate Professor*
- Dr. P. Dunscombe, *Assistant Professor*
- Dr. G. Froese, *Assistant Professor*
- Dr. P. Hahn, *Assistant Professor*
- Dr. D. I. Hodson, *Assistant Professor*
- Dr. W. Huda, *Assistant Professor*
- Dr. W. McLellan, *Assistant Professor*
- Dr. A. L. Meikle, *Assistant Professor*
- Dr. R. F. Palser, *Assistant Professor*
- Dr. A. Sourkes, *Assistant Professor*
- Dr. T. Lee, *Lecturer*

Department of Surgery
- Dr. E. Ramsey, *Professor*
- Dr. B. J. Anderson, *Assistant Professor*
- Dr. W. Beecroft, *Assistant Professor*

Department of Social and Preventative Medicine
- Dr. N. W. Choi, *Professor*
- Dr. N. A. Nelson, *Associate Professor*
- Mrs. P. F. Moodie, *Lecturer*

Faculty of Science

Department of Physics
- Dr. P. Dunscombe, *Adjunct Professor*
- Dr. G. Froese, *Adjunct Professor*
- Dr. W. Huda, *Adjunct Professor*
- Dr. L. Lee, *Adjunct Professor*
- Dr. R. Palster, *Adjunct Professor*
- Dr. S. Shalev, *Adjunct Professor*

Computer Science
- Dr. M. Laucht, *Associate Professor*

RADIATION ONCOLOGY

Acting Director — K. Malaker, M.D., Ph.D.

HEALTH SCIENCES CENTRE:

B. J. Anderson, M.D., F.R.C.S.(C)
W. A. Beecroft, M.D., F.R.C.S.(C)
J. M. Gillies, L.R.C.P.&S.(E), F.R.C.P.(C), F.A.C.R.
P. Hahn, M.D., Ph.D.
D. I. Hodson, M.A., B.M., B.Ch., F.R.C.P.(C)
W. McLellan, M.B., Ch.B., D.M.R.T., F.R.C.P.(C)
A. L. Meikle, M.B., Ch.B., D.M.R.T.(Ed.), F.R.C.P.(C)

Resideats

A. Bains, M.D., K. Vijayaraghavan, M.B., B.S., G. Wong, M.B., B.S.

Radiobiology

S. Biswas, Ph.D. — Honourary Research Associate
R. M. Das, B.Sc., Ph.D.

Support Staff

C. Campbell, J. Demeulemeester

Orderlies:

J. Pelletier, D. Perreta, R. Villabrille

ST. BONIFACE HOSPITAL UNIT

Support Staff

C. Einarson, K. Friesen, S. Johnson, L. Love, L. Soshycki, N. VanHorne, A. Werbicki

THERAPY EQUIPMENT

Health Sciences Centre:

Therac 40/Sagittaire linear accelerator
4 MV S.H.M. linear accelerator
A.E.C.L. Model F Cobalt 60 beam therapy unit
250 kV x-ray therapy unit
140 kV x-ray therapy unit
Picker simulator
A.E.C.L. Therasim 750 simulator
A.E.C.L. Theraplan treatment planning computer
TAGMED 2450 MH_z hyperthermia unit

St. Boniface Hospital:

100 kV superficial x-ray therapy unit
A.E.C.L. Theratron 780 Cobalt unit

EXTERNAL IRRADIATION

At the Oncology Centre, 1,232 new patients were treated and 718 were re-treated.

At St. Boniface Hospital, 389 new patients were treated and 155 were re-treated.

	H.S.C.	S.B.G.H.	Total
Patient Visits	18,933	3,057	**21,990**
Treatments	25,232	6,287	**31,519**

NUMBER OF TREATMENTS WITH RADIOACTIVE SOURCES

	Cesium 137	Gold Grains	Iridium Mould	Iridium Implants	Beta Applicator	Total
H.S.C.	128	0	7	7	20	**162**
S.B.G.H.	0	0	0	0	3	**3**
Total	**128**	**0**	**7**	**7**	**23**	**165**

INTRODUCTION

The Radiation Oncology Service is based at the Cancer Foundation, to which the majority of patients are referred and where major therapy facilities are located. However, with the opening of the extension of the Cancer Treatment Facility at St. Boniface Hospital, the scope of Radiation Oncology has increased. A new A.E.C.L. Isocentric Cobalt Unit, which was installed one year ago, offers superior quality of treatment as compared with the previous Eldorado Therapy Unit. Since the extension of the cancer treatment facility at St. Boniface Hospital, Radiotherapy consultation, follow-up and other radiotherapy related services have increased and, to meet the need, a simulator has been purchased and is being installed at the St. Boniface Radiotherapy Unit. Each staff member continues to rotate through the St. Boniface Unit. This arrangement has made greater integration possible between the Foundation and St. Boniface Hospital Radiotherapy Services.

In addition, members of the professional staff regularly attend Tumor Rounds at Victoria General Hospital and Misericordia Hospital. At the Cancer Foundation, a Head and Neck Multidisciplinary Clinic takes place weekly and is reported in detail elsewhere. Multidisciplinary Lung Consultation sessions are also held weekly. Multidisciplinary G.I. Tract Consultation sessions have begun. Surgical Oncology Clinics are held twice weekly and an increasing use is being made of the Procedures Room for minor surgical procedures. The staff maintain a very close liaison with Gynecological Oncology. Intracavitary insertions of cesium are confined to the Health Sciences Centre. Increasing numbers of interstitial implants are also carried out at the Health Sciences Centre.

There has been an increase in academic activity and participation by this Unit since reorganization. This includes an upgraded Residency Training Program. The Department also takes an active part in Undergraduate Teaching. The Department offers a four year

Residency Training Program in Radiation Oncology, which is approved by the Royal College of Physicians and Surgeons of Canada and the American College of Radiology. The Department also offers a two year training program in Radiotherapy Technology, which continues to attract a very large number of well qualified applicants.

BRACHYTHERAPY

Until last year all the brachytherapy, including interstitial implant, patients were admitted to D2 in the General Centre. This year brachytherapy beds have been relocated to B6. Due to this change, the number of beds has been reduced from four to two although we continue to occupy two rooms in the B6 ward. Special shielded beds, designed and built by the Medical Devices at the Foundation, proved to be extremely useful. A special mechanical mobile activity lead shield which we found to be most useful, also has been designed and installed by the Section of Medical Devices.

ACADEMIC ACTIVITIES

1. *Radiation Oncology Clinical Conference:* new referrals and new problems are discussed twice weekly.
2. *Radiotherapy and Radiology Seminars:* CT Scans for diagnosis and Radiotherapy Treatment Plans are discussed. Dr. W. Gordon and Dr. H. Greenberg, members of the Department of Radiology, participate regularly.
3. *Radiotherapy Treatment Planning Seminars:* are held once monthly.
4. *Monthly Lecture Sessions:* once each month members of our Department, or invited guests from other facilities, present a topic of current medical or oncologic interest. Residents also participate in these lectures.
5. *Residency Training Program:* currently we have three residents in training, Dr. K. Vijay, after completing one year of Internal Medicine rotation, returned to Radiation Oncology for her 4th year of training. She has been appointed as Senior Resident responsible for Resident administration. Dr. A. Bains started his one year of Medical Rotation in July and will return to Radiation Oncology in July 1986. Dr. G. Wong joined us in January 1985, having had two years of training in Hong Kong.

POSTGRADUATE TEACHING

Dr. Malaker, Dr. Hodson and Dr. McLellan presented a series of seminars on the Principles and Practices of Radiotherapeutics to residents from Surgery, Gynecology, and Chest Medicine.

UNDERGRADUATE TEACHING

1. *4th Year Medical Elective Program* — This year we had a total of 17 fourth-year students who rotated through Radiation Oncology as part of their Radiology rotation. Dr. Hodson and Dr. Malaker lectured on Radiation Physics and Radiation Biology to these students.
2. *2nd Year Medical, Clinical Skills Teaching* — For the first time Radiation Oncology took the responibility of teaching Clinical Skills to 2nd year students. Between January and

May 1985, 47 2nd year students rotated through Radiotherapy as part of their Clinical Skills program.

OTHER ACADEMIC ACTIVITIES

Conference on Nutritional Management of Cancer Patients

A day long conference was organized by the Radiotherapy Department with financial assistance from Mead Johnson and Ross Laboratories. Dr. Maurice Shils, Head of Nutritional Services, Memorial Sloan-Kettering Hospital and Professor of Medicine, State University of New York, was the guest speaker. He presented "How Cancer Patients Become Malnourished" and "Current Status and Future Prospects of Nutritional Support of Cancer Patients". Apart from Dr. Shils, members of the Radiotherapy Department, Department of Surgery and members of the T.P.N. Unit took an active part in the symposium.

Invited Lecturer

In June 1985 Dr. K. Malaker was an invited lecturer on the Concepts in Brachytherapy at the Gustave Roussy Cancer Institute, Villejuif Cedex, Paris, France.

PARTICIPATION IN NATIONAL AND INTERNATIONAL CONFERENCES

1. 37th Annual Midwinter Radiological Conference in Los Angeles and the Midwinter Oncology Conference: Post Conference Seminar in Kauai, Hawaii — Dr. K. Malaker.
2. Canadian Association of Radiologists in Toronto — Dr. J. M. Gillies, Dr. P. Hahn and Dr. K. Malaker.
3. IV World Conference on Lung Cancer in Toronto — Dr. D. I. Hodson.
4. Royal College of Physicians and Surgeons of Canada in Vancouver — Dr. J. M. Gillies.
5. American Society of Therapeutic Radiology and Oncology in Miami — Dr. P. Hahn.
6. American Association for Cancer Education in San Francisco — Dr. K. Malaker.

CLINICAL AND BASIC RESEARCH: HYPERTHERMIA

Dr. K. Malaker, Dr. P. Dunscombe, Dr. G. Froese

We have continued to accept patients with superficial tumors on low dose radiation and daily hyperthermia. Control and patient compliance and toxicity remain satisfactory in appropriate cases with superficial tumors. We have also started to treat patients as a pilot project, using 2250 MHz microwave system for superficial tumors not deeper than 3 cm. from the skin surface and superficially not more extensive than 6 cm. in diameter. A protocol has been designed for this pilot work.

SUPERFRACTIONATED AND MULTIPLE DAILY FRACTIONATED RADIOTHERAPY

Dr. K. Malaker, Dr. D. I. Hodson, Dr. A. L. Meikle, Dr. W. McLellan, Dr. J. M. Gillies

Superfractionated radiation research in a clinical setting continues to accrue patients in several sites.

Advanced Head and Neck Cancer:

Advanced head and neck cancer has been treated with twice daily fractions at the rate of 180 rads per fraction; each fraction is given at five to six hour intervals and the total dose is up to 5400 rads. The tolerance is satisfactory and early tumor control seems to be superior to standard fractionation; tolerance toxicities and tumor control are being evaluated.

Carcinoma of the Pancreas:

Superfractionated treatment of pancreatic cancer is now in its third stage. The patients are receiving 160 rads per fraction with fractions given at 5-6 hour intervals to a total dose of 4800 to 5400 rads. The early tolerance and immediate control seem to be satisfactory. Long term control and delayed reactions for this site are currently being evaluated.

Carcinoma of the Esophagus:

Inoperable, localized esophageal carcinoma is being treated with a multiple fractionated schedule. Time, dose, fractionation are 180 rads per fraction, 2 treatments per day at 5-6 hour intervals to a total dose of 5250 rads. The short-term response and tolerance seem to be satisfactory; the accrual for this pilot project is rather slow because of the low incidence, but the trial continues.

Radical Combined Surgery/Radiotherapy Sandwich Technique for Operable Ca Esophagus:

We continue to accrue patients slowly in this pilot study. This technique which uses pre-operative 600 rads single dose radiotherapy to the esophagus to be followed by esophagectomy within 24 hours of radiation. This is to reduce operative metastasis and slow the rate of the residual tumor cell growth in the mediastinum. After 2-4 weeks of convalescence, providing pathological staging remains unaltered, post-operative radiation is given to the mediastinum to a total dose of 4000 rads in 15 treatments, 800 rads to the upper abdomen, paraceliac and hepatic region, and 700-750 rads to both paraclavicular areas. There have been no serious complications from this regimen and the short-term survival (24 months) may be superior to other regimens.

RADIOPROTECTIVE EFFECT OF SUPEROXIDE DISMUTASE

Dr. K. Malaker, Dr. D. I. Hodson, Dr. V. Taraska

The radioprotective effect of copper zinc superoxide dismutase, named Winsod, which will be supplied by the Rh Institute of Manitoba, will be tested on patients with carcinoma of the lung who have been accepted for radical treatment. This work has again been funded by the Manitoba chapter of the Canadian Lung Association.

THE INVESTIGATION OF DELAYED RADIATION REACTION

Dr. K. Malaker

We will continue to accrue, register and document all the patients with significant delayed radiation reactions, i.e. neuropathy, fibrosis, nephritis, etc. On satisfactory accrual in this series, following analysis, it is hoped that the findings will lead to the investigation of genetic response to radiation reaction.

LABORATORY INVESTIGATIONS:

Dr. R. M. Das, Dr. K. Malaker and Dr. G. Froese continue to work on the radiobiology of multiple fractionated radiation, the radioprotective effect of superoxide dismutase, and normal tissue reaction to hyperthermia with and without radiation in the animal system. These investigations have been funded by the Manitoba Cancer Foundation. Preliminary findings have been reported at the 47th Annual General Meeting of the Canadian Association of Radiologists in Vancouver and further follow--up studies have been presented at the 48th Annual General Meeting of the Canadian Association of Radiologists in Toronto, in June 1985.

Dr. Per Hahn is continuing on a project with Dr. S. Shalev in the optimization of treatment for prostate cancer and Dr. S. Shalev, along with Dr. K. Malaker, has initiated studies of digital enhancement of port films.

HEAD AND NECK TUMOR CONFERENCE AND CLINIC

Dr. D. Ian Hodson — Co-ordinator

The weekly Head and Neck Clinic, was established in 1971. Each Thursday morning staff members from the Manitoba Cancer Treatment and Research Foundation and the Health Sciences Centre, with a special interest and expertise in head and neck oncology, convene. Walk-rounds are held where current in-patient problems are reviewed, following which the formal Conference begins. The relevant pathology and radiology is then reviewed, following which discussion takes place aimed at producing a consensus of opinion, in a multidisciplinary setting, for the optimum management course for each patient. The follow-up clinic is held following this Conference. Here, both previously treated patients and often patients undergoing treatment are reviewed, again in a multidisciplinary fashion, allowing the treatment results and complications of all modalities to be appreciated.

The Conference and Clinic continue to be extremely busy with 190 patients being presented at the formal Conference and a total of 1,323 patient visits being recorded in the follow-up clinic. Once more this represents an increase over the previous year. We would like to thank the nursing and administrative staff for their help in organizing this weekly undertaking.

The formal Conference presentations continue to be chaired in rotation by representatives of the Radiation Oncology and Surgical Sections. This system was introduced in 1981 and appears to be successful, allowing greater participation by individual physicians and encouraging clinical co-operation. We would like to take this opportunity to thank Drs. MacEwan and Alguacil for their invaluable help with the Radiology and Pathology portions of the Conference.

Unfortunately patients with advanced non-resectable disease continue to form a substantial proportion of patients seen and we are continuing with our participation with the Princess Margaret Hospital in Toronto in the prospective evaluation of the addition of chemotherapy (5-Fluorouracil and Mitomycin-C) to radiotherapy for these patients. The Head and Neck Clinic is also active in the prospective local investigation of the use of multiple daily fractions of radiation and hyperthermia.

PUBLICATIONS

Feld, R., Evans, W. K., Coy, P., Hodson, D. I., McDonald, A. S., Osaba, D., Payne, D. G. and Pater, J. L.: Canadian Multicentre Randomized Trial Comparing Sequential and Alternating Administration of Two Non-cross Resistant Chemotherapy Combinations in Patients with Limited Small Cell Carcinoma of the Lung. In the Proceedings of the 21st Annual Meeting of the American Society of Clinical Oncology, Houston, May 1985.

Wong, G., Hodson, D. I., Malaker, K.: The Long-term Results of the Pilot Study for the Treatment of Advanced Unresectable Head and Neck Tumors by Combination Chemotherapy and Split Course Radiotherapy, Journal of Otolaryngology, November 1985.

PRESENTATIONS

Rapid Ultrasensitive Method for Analyses of Imino Acids in Connective Tissues. Presented at Int. Assoc. for Dental Research, Las Vegas, Nevada, March 1985: K. Malaker, S. Biswas.

Clinical Microwave Hyperthermia at 2450 MHz. Presented at C.A.R. Meeting in Toronto, June 1985: P. Dunscombe, K. Malaker.

Stem Cell Radioprotection by Superoxide Dismutase in Animal Systems. Presented at C.A.R., Toronto, June 1985: K. Malaker, R. M. Das.

Primary Lymphoma of Central Nervous System. Presented at C.A.R., Toronto, June 1985: K. Malaker.

Superfractionated Radiotherapy & Combination Chemotherapy in the Treatment of Limited Oat Cell Carcinoma of the Bronchus. Proceedings of the 4th World Conference on Lung Cancer, Toronto, August 1985: D. I. Hodson, M. Levitt, K. Malaker, A. L. Meikle.

SURGICAL ONCOLOGY

SECTION MEMBERS:

W. A. Beecroft, D.D.S., M.D., F.R.C.S.(C), F.A.C.S.,
B. J. Anderson, M.D., F.R.C.S.(C)

RESIDENTS:

Sam Beenken, M.D., Joseph Dort, M.D., Kiu-Sing Cheng, M.D., Mark DeGroot, M.D.

NURSING STAFF:

J. Kostenuik, R. N., L. Suggitt, R.N., S. Kelly, L.P.N.

SECTION OF SURGICAL ONCOLOGY ORGANIZATION

The Section of Surgical Oncology continued to develop in 1985. Daily consultative service is provided and clinics are held four days a week at The Manitoba Cancer Treatment and Research Foundation. Active involvement in the Head and Neck Tumor Conference and Clinics continues. Biopsy and endoscopy services are provided. Sigmoidoscopy, nasendoscopy and fiberoptic laryngoscopy capability for patient evaluation and follow-up at the Foundation is available.

Frequent multidisciplinary consultations with Radiation Oncology and Medical Oncology are carried out. Surgical procedures, both diagnostic and therapeutic are carried out at the Health Sciences Centre as part of the Green Surgery Service function in the Section of General Surgery.

TEACHING

The resident and undergraduate house staff from the Green Surgery Service at the Health Sciences Centre are participants in the Head and Neck Tumor Conference and Clinic as well as the other Surgical Oncology clinics. Each year two senior General Surgical Residents as well as two junior Otolaryngology Residents participate in the clinics as part of their postgraduate surgical training program. Other junior General Surgical Residents as well as Oral Surgery and off service residents participate from time to time. These clinics provide experience in new patient evaluation, multidisciplinary consultation, and patient follow-up in a wide variety of malignant diseases. Formal ward rounds in the Head and Neck Unit at the Health Sciences Centre as well as a lecture series in Head and Neck Oncology is provided.

CLINICAL INVESTIGATION

Active participation in the numerous N.S.A.B.P. Breast Carcinoma Trials is promoted. Patients who are willing to participate and are eligible for these trials are entered if feasible. The N.C.I.C. M.E.5 Malignant Melanoma Trial to evaluate excision margins and regional node management is ongoing, but to this stage accrual has been poor. Patient accrual in the advanced laryngeal or hypopharyngeal trial looking at radiation versus radiation plus chemotherapy has been good. Other new Head and Neck carcinoma protocols are now being developed and hopefully patient accrual can be initiated in the near future.

A retrospective chart analysis evaluating the results of the management of laryngeal carcinoma was initiated and is ongoing. This will provide a baseline to compare results with other centres as well as evaluate any new treatment modalities implemented.

SECTION OF SURGICAL ONCOLOGY STATISTICS

Manitoba Cancer Treatment and Research Foundation

	New Patients	Follow-up Visits	Total Patient Visits
1983	217	784	1,001
1984	287	1,225	1,512
1985	417	1,660	2,077

Diagnostic Outpatient Procedures

	Endoscopy	Biopsy	Total
1983			152
1984	11	182	193
1985	36	247	283

PUBLICATIONS

Symposium: Staying Out of Trouble in Head and Neck Surgery. Robins, R. E., Young, J. E. M., Archibald, S. D., Rotstein, L., Rosen, I. B., Beecroft, W. A., Beahrs, O. H., Annals R.C.P.S.C., Vol. 18, No. 1, January, 1985.

PRESENTATIONS

"The Role of Modified Neck Dissection in Well Differentiated Thyroid Cancer", The Royal College of Physicians and Surgeons Meeting, Montreal, P.Q., B. J. Anderson.

"Nutritional Options in Oncology — An Overview", Nutrition Problems in Oncology, Symposium, Winnipeg, Manitoba, April, 1985, B. J. Anderson.

"Deglutition Problems in the Head and Neck Cancer Patient", Nutrition Problems in Oncology, Symposium, Winnipeg, Manitoba, April, 1985, W. A. Beecroft.

"The Use of Cricothyroidostomy in Head and Neck Surgery", The Eastern Great Lakes Head and Neck Oncology Association, Buffalo, New York, November, 1985, W. A. Beecroft.

"Carcinoma of Larynx: The Manitoba Experience", American College of Surgeons, Manitoba Chapter, Winnipeg, Manitoba, December, 1985, J. Dort, W. A. Beecroft, B. J. Anderson.

ONCOLOGY NURSING/TECHNOLOGY

Director of Nursing: B. Glenday, R.N., R.T.T.
Assistant Director of Nursing and Clinical Investigation Liaison Nurse: J. Lutz, R.N.

MEDICAL ONCOLOGY:

N. Johnson, R.N., Senior Nurse
S. Bracken, R.N., L. Friesen, R.N., D. Rumpel, R.N., S. Switzer, R.N.

Clinical Assistants:
I. DeSousa, G. Harney, L. Jonasson, U. Merck

Clinical Investigation:
K. McDonald, R.N., Senior; V. Powell, R.N.

Gynecological Oncology:
I. Chrunyk, R.N.

Pediatric Oncology:
P. Pruden, R.N.

RADIATION ONCOLOGY:

M. Chambers, R.N., Senior Nurse
B. Dodds, R.N., S. Kelly, L.P.N., J. Kirbyson, R.N., R.T.T., L. Scott, R.N.

Clinical Assistants:
B. Babcock, E. Egan, A. Pope, I. Turnbull

Unit Assistant:
M. Corden, I. Turnbull

Surgical Oncology:
J. Kostenuik, R.N.

Radiotherapy Technologist Training Program Coordinator:
E. Kirk, R.N., A.C.(T)

Radiotherapy Technologists:
Supervisor — V. Pruden, R.N., R.T.T.
Senior Technologists — S. Ryder, R.T.T., T. Sydorchuk, R.T.T., J. Wood, R.T.T.
Technologists — H. Doherty, R.T.T., K. Fox, R.T.T., J. Grestoni, R.T.T.,
J. Lamb, R.T.T., S. Mehta, R.T.T., P. Sparkes, R.T.T., D. Swanson, R.T.T.,
T. Walker, R.T.T., D. Wells, R.T.T., G. Winski, R.T.T.

Student Radiotherapy Technologists:
B. Bevis, T. Erwin, D. Hughesman, K. Patterson, K. Wedlake (Second Year)
T. Corkum, T. DePape, S. Iftody, R. Kubisch, C. Speiss (First Year)

ST. BONIFACE NURSING AND TECHNOLOGY STAFF:

G. Ogilvie, R.N., R.T.T., Senior Nurse
S. Hatton, R.N., R.T.T., B. Lucko, R.N., R. Olson, R.N., R.T.T.,
S. Sharpe, R.T.(R&T).

ONCOLOGY NURSING/TECHNOLOGY

Excellence in nursing practice is a goal that the Department of Nursing strives to attain. To achieve this result, the Department has placed a strong emphasis on educational programs for all staff members. Attendance at National, International and local symposia is encouraged and the MCF was represented at the Oncology Nursing Society, 10th Annual Symposium, Houston, Texas; The Third National Oncology Symposium, Edmonton, Alberta; The Psychosocial Oncology Conference, Calgary, Alberta and the Society of Gynecological Oncology Nurses Conference, Atlanta, Georgia; as well as local educational programs.

We are delighted that Janice Lutz, ADON, is on the Executive Committee of the newly formed Canadian Oncology Nurses Organization. At the local level, MCF nursing staff is active in the Manitoba Oncology Nurses Interest Group and Jeannette Kostenuik, of this staff, has produced the first newsletter for the Interest Group.

We have established that Oncology/Surgical Nursing Conjoint Rounds are necessary to provide continuity of care and improved follow-up. Weekly nursing rounds are planned.

Social Service Rounds continue to provide much needed intervention for patients. Because of the success of Social Service Rounds, the nursing staff will be instituting rounds with the Home Care Department. This should help us get services into the patients' homes much faster and at an earlier stage in their disease.

The Health Sciences Centre, School of Nursing, has rotated their senior students through the Medical Oncology area as part of their psychosocial training. The students and patients have benefitted by the interaction and it has proved to be a very rewarding part of the nurses' educational experience.

The University of Manitoba, School of Nursing, has sent students for both pediatric and senior experience.

Patient education is a primary nursing responsibility and the nursing staff, from all areas , devote a great deal of time in this endeavor. A joint committee of St. Boniface, HSC and MCF Medicine, Nursing and Pharmacy has worked to set up standard guidelines for the care of central lines and implantable ports. This committee has also standardized teaching programs for patients caring for these devices. Nursing staff also do ongoing teaching on the care of continuous infusion pumps.

Safe mixing, handling, administration and disposal of antineoplastic agents is a concern of the MCF nursing staff. A committee of MCF Nursing staff, Pharmacy representatives and HSC and St. Boniface Nursing is updating the guidelines for handling antineoplastic agents.

Our nurses and technologists continue their commitment to be involved in other educational activities. They are often guest speakers at urban and rural institutions, and also participate in informative tours of the Foundation.

Our Clinical Nurse Specialist provides valuable assistance to Medical Oncologists in clinical evaluation, furnishing the necessary liaison between patient care and clinical investigation management and evaluation. She is actively involved in symptom control, clinical trials and, monitors patients entered into the Pain Control and Antiemetic Studies. The clinical trial addressing pain control and its side effects studied a comparison of sustained release morphine tablets with morpine syrup. The antiemetic study evaluated Droperidol by

IV infusion as a means of controlling nausea and vomiting associated with chemotherapy.

The Oncology Nursing Workshop, now coordinated by J. Lutz, expanded from a two-day to a three-day seminar and was held on four occasions, with a total of 112 participants. This program is available to all interested nurses as a continuing education seminar. However, its main thrust is to provide information for those nurses already working in the field of Oncology, as well as to prepare those planning to enter the field of Oncology nursing. The three-day theory program is followed by a three-week practicum, for those nurses entering the specialty, where they are provided the necessary expertise in safe antineoplastic drug administration and handling.

The Technologists give competent and empathetic care to our patients to whom they are very committed. They are very good at patient teaching and even with an increased workload, coupled with the complex treatments of today, still find time for those little extras that add to the quality of life for patients.

RADIOTHERAPY TECHNOLOGIST TRAINING PROGRAM

E. Kirk

Together with Red River Community College, the Foundation continues to provide those persons interested in a career in the health care specialty of oncology, the opportunity to train and become certified in the field of Radiation Technology.

The Radiotherapy Technologist Training Program continues to change in response to needs identified by the cancer patient, technological advances, and the students themselves. As we strive to provide the optimum learning environment for the students enrolled in this Program, we acknowledge that this is the only way in which we can equip the practicing technologist with the skills necessary to provide competent, empathetic care for our patients.

Five graduates of our Program wrote the C.A.M.R.T. National Certification Examination in 1985. Our congratulations to Heather Doherty, Sherri Hein, Karen McDuffe and Debbie Swanson. Special congratulations to Karen, who was the recipient of the Picker Award, for general proficiency in Radiotherapy Technology, and to Debbie, who won the annual M.A.M.R.T. student essay competition.

1985 saw the Education Program Committee develop a Refresher Program for Radiotherapy Technologists who have been out of the field for longer than 5 years. One candidate progressed through this Program, and the Committee is now in the process of evaluating its effectiveness.

As of December 1985, we had ten students enrolled in the Radiotherapy Technologist Training Program. Interest in the program continues to grow with over 60 persons applying for the five student positions available this year.

My personal thanks to those staff members who continue to give of their time and expertise, not only in the classroom but also in the clinical setting, in order to ensure the continuing high quality of graduates of this Program.

MEDICAL ONCOLOGY

Director — David M. Bowman, M.D., B.Sc.(Med), F.R.C.P.(C)

MEDICAL ONCOLOGISTS

L. Brandes, M.D., B.Sc.(Med), F.R.C.P.(C)
J. Foerster, M.D., B.Sc.(Med)
G. Goldenberg, M.D., Ph.D., F.R.C.P.(C)
L. G. Israels, B.A., M.D., M.Sc., F.R.C.P.(C)
J. Johnston, M.B., F.R.C.P.(C)
M. Levitt, M.D., M.Sc., F.R.C.P.(C)
B. Schacter, M.D., B.Sc.(Med), F.R.C.P.(C)

CLINIC ASSISTANT

L. Pratt, M.D.

CLINICAL FELLOWS

R. Nash, M.D., T. Nijjar, M.D.

RESIDENTS

C. Bradley, W. Cameron, C. Cheema, J. Hurwitz, F. Karlicki, C. Rihal, A. Thakkar, K. Van Ameyde, B. Zanke

NURSING STAFF

N. Johnson (Senior Chemotherapy Nurse)

Clinical Nurses

S. Bracken, I. Chrynuk, L. Friesen, D. Rumpel

Nursing Aides

I. De Sousa, G. Harney, L. Jonasson, U. Merck

CLINICAL INVESTIGATION OFFICE

Director — Dr. M. Levitt, M.D., M.Sc., F.R.C.P.(C)
Protocol Nurse Co-ordinator — J. Lutz, R.N.
Protocol Nurse: K. McDonald, R.N.

Protocol Technicians

K. Hjalmarsson-Taylor, E. Janke, H. Kampen, E. Stiles, H. Whitaker

Clinic Receptionist

C. Jones

Departmental Secretaries

J. Powell, T. Reutcky

*See also report of "Oncology Unit — St. Boniface General Hospital."

MEDICAL ONCOLOGY*

ORGANIZATION

The Manitoba Cancer Treatment and Research Foundation Department of Medical Oncology provides programmes for diagnosis and management of adults with neoplastic and hematologic diseases in Manitoba. Patients are also referred from neighbouring provinces and states. Facilities are maintained geographically at the Foundation and at St. Boniface General Hospital (See also report of "Oncology Unit — St. Boniface General Hospital"). The Foundation also coordinates a Cancer Outreach Programme to provide rural patients and their families with optimal standards of care close to their home environment. All Medical Staff have full-time appointments at the University of Manitoba and most are actively conducting programmes of basic research and/or clinical investigation.

The Oncology Centre at the Foundation is an Outpatient facility also housing the research programmes of the Manitoba Institute of Cell Biology, such that basic research, clinical investigation and patient care programmes are intimately related. The Department of Medical Oncology includes eight medical oncologists who provide care for patients with malignant and hematologic diseases. In addition, close liaisons with radiation oncology, gynaecological, urological and surgical oncology, plus pediatric oncology are maintained. The professional team includes oncology nurses specialized in parenteral administration of chemotherapy and immunotherapy. The Radiation Oncology service is also located within the Oncology Centre, thus, facilitating interdisciplinary approaches to cancer care. A hematology laboratory at the Oncology Centre provides hematologic data of high quality promptly and efficiently to all of the clinics as is essential to the ongoing care of both urban and rural patients. During 1985, installation of a fully automated Coulter S-plus IV blood counter and printer unit occurred. Other patient services in the Oncology Centre include a special cancer-oriented Social Service, and Epidemiology and Statistics Section. These outpatient services are integrated with the inpatient services of the adjacent Health Sciences Centre. Thus, when necessary, patients are admitted to the clinical teaching units of the General Centre (HSC). Here they are cared for by the House Officers and the Oncology Fellows under the supervision of the senior consultant of the Medical Oncology Service. The Medical Oncology Service also provides the Hematology/Oncology consulting service to inpatients of the Health Sciences Centre.

TEACHING

In addition to the service component involved in care of ambulatory patients with neoplastic disease, the Medical Oncology Service provides teaching for students at an Undergraduate level through lectures in Hematology and Oncology, and a laboratory hematology course; and at the graduate level of Interns and Residents in the Department of Medicine. Full-time Clinical Fellows and residents in Internal Medicine rotate on the Hematology/Oncology Service, both at the Health Sciences Centre and St. Boniface Hospital. In addition, they participate in the Clinical and Research Seminars and Rounds of the Department as well as resident Clinical Seminars. All third year undergraduate medical students at the University of Manitoba are given a series of Hematology case reviews under the supervision of various members of the Attending Staff and the Hematology fellows. Some of the fourth year medical students also participated in one-month selectives on the Hematology/Oncology Service. The Hematology/Oncology Morphology Teaching Laboratory under the direction of Ms. A. Sasyniuk, R.T., B.Sc., participates fully with the Medical Oncology Department

including the St. Boniface Hospital Unit, in the teaching of Medical and Pediatric fellows and rotating residents, as well as the fourth year clerks and third year clerks participating in the Hematology/Oncology electives.

The purpose of this laboratory is to:

1. Coordinate the clinical teaching with the laboratory data.
2. Train fellows, residents and clinical clerks in the Hematology/Oncology programme to interpret the morphology of the peripheral blood and bone marrows obtained from patients they have seen in clinic or admitted to hospital.
3. Give each clinical clerk during their elective a caseload of patients, representative of the spectrum of ages in normal and disease states. Therefore, providing students with experience to develop efficiency in obtaining relevant history, to recognize life threatening problems and to establish priorities in management in acute and chronic situations.

The schedule provides 4-6 hours/week training in examination of morphology and interpretation of peripheral blood smears, bone marrows and biopsies on a one to one basis. Each student has the opportunity to examine the above material at the time of diagnosis, during treatment, and during remission.

For those who choose to rotate through this program the major emphasis of this laboratory is to integrate and to broaden the understanding in Hematology/Oncology. It also provides an opportunity to gain first hand experience at interpretation of peripheral blood smears and bone marrow smears and a more fuller utilization of useful diagnostic tests.

During 1985 the rotation included 8 trainees in pediatrics, 10 trainees in internal medicine, 19 selective/elective undergraduate student trainees and trainees in pathology. The excellent teaching in the laboratory is provided by Anne Sasyniuk, assisted by Bette Jacobucci. The program is an important complementary experience for physicians in pediatrics or Internal Medicine who will be providing health care in urban or rural centres, as well as those who will pursue an academic career.

During 1985, stimulating speakers on our Visiting Professor Programme included Doctor W. Schain of the National Cancer Institute (USA) speaking on "Psychosocial Aspects of Breast Cancer Surgery," Doctor B. W. Brown, Stanford Medical School, speaking on "Clinical Trial Design," and Doctor L. Weiss, Roswell Park Cancer Institute, speaking on "Cancer Metastases." Ongoing support of the programme by ICI Pharma is gratefully acknowledged.

BASIC RESEARCH

The clinical facility on the ground floor of the Oncology Centre is intimately juxtaposed with the Manitoba Institute of Cell Biology which is situated on the second floor of the same building. This relationship allows sophisticated tests and expert consultations to be immediately available from laboratories doing research in tumour immunology, blood coagulation, molecular biology, and membrane transport of chemotherapeutic agents. Please see the separate report of the Manitoba Institute of Cell Biology for descriptive details.

CLINICAL INVESTIGATION

New developments in medical therapy of cancer have made the conduct of a clinical investigation programme the cornerstone of developing cancer treatment programmes. In Medical Oncology, programmes of clinical investigation are carried out both on an independent basis, and in collaboration with major clinical trial co-operative groups.

The Protocol Review Committee, with multidisciplinary membership evaluates and approves all new clinical protocols involving the Manitoba Cancer Treatment and Research Foundation patients. Committee membership includes Doctors M. Levitt (Chairman), D. Bowman, B. Weinerman, K. Malaker, G. Krepart, M. Kobrinsky, and L. G. Israels.

The Department of Medical Oncology also participates in clinical trials sponsored by several national and international clinical trial co-operative groups, including the National Cancer Institute of Canada (NCIC — Principal Investigator — Doctor M. Levitt), and the National Surgical Programme for Breast and Bowel Cancers (NSABP — Principal Investigator, Doctor D. M. Bowman). Participation in numerous protocols with these co-operative groups and institutions remains a high priority of medical oncology. We believe these multi-institutional co-operative trials represent the forefront of developmental cancer therapeutics. Table I, which follows, indicates our participation in these protocols during recent year.

During 1985, a Data Quality Assurance Monitoring Committee was established to monitor the quality of accruing data on all approved protocols. This committee is being chaired by Doctor D. Bowman in its formulative phase, and has member representation by all of the Foundation's clinical departments.

During the year, the Department of Medical Oncology was also pleased to host a one-day workshop on "Dose Intensification Protocols in Breast Cancer," chaired by Doctor W. Hryniuk, Director of the Hamilton Clinic of the Ontario Cancer Treatment and Research Foundation.

TABLE I

CLINICAL INVESTIGATIVE PROTOCOL ACCRUAL

Study Group	1984	1985
NCIC		
Remaining On-Study from prior years	286	341
New Patient Accrual	106	69
Off Study	51	73
Remaining On-Study	341	337
NSABP		
Remaining On-Study from prior years	271	314
New Patient Accrual	59	55
Off Study	16	22
Remaining On-Study	314	347
*LOCAL TRIALS**		
Remaining On-Study from prior years	33	45
New Patient Accrual	35	48
Off Study	23	35
Remaining On-Study (year end)	45	58
Total On-Study (year end)	**700**	**742**

*1985 includes 8 prostate protocol patients entered in 1984, but not previously (1984 Report) documented.

Additional supportive care studies (sustained release morphine and droperidol trials) accounted for a further 4 patients on-study during 1985.

The following is a brief description of active clinical investigative trials.

Disease Site	Number	Description
Ovarian Carcinoma	NCIC OV.6	Non-randomized study to determine the efficacy of surgery alone in patients with Stage IA or Stage IB disease when extensive surgical staging has been done to confirm limited disease.
	NCIC OV.7	To compare current optimum chemotherapy with abdominopelvic irradiation in Stage IC, IIA, B, C, or III, with microscopic disease. 1. RT to abdomen x 22 treatments and RT to pelvis x 11 treatments VERSUS 2. Cyclophosphamide I.V. and Cis-Platinum I.V. q4 weeks x 9 courses.
	NCIC OV.8	To compare Carbo-platin plus Cyclophosphamide versus Cis-Platinum plus Cyclophosphamide in patients with macroscopic residual disease. Responders receive 3 more courses of original chemotherapy versus RT to abdomen x 22 treatments and RT to pelvis x 11 treatments.
Lung Carcinoma	NCIC BR.4	To compare standard versus alternating non-cross resistant chemotherapy in "extensive" small cell carcinoma. 1. Cytoxan i.v., Adriamycin i.v., Vincristine i.v. day 1 only q3 weeks x 6 courses VERSUS 2. CAV (above) cycles 1, 3, 5 alternating with VP-16 i.v. and Cis-Platinum i.v. daily x 3 days cycles 2, 4, 6. Cycles are q3 weeks x 6 courses.
	NCIC BB.5	To compare two chemotherapy regimens and to evaluate changes in "Quality of Life". 1. Vindesine day 1, weekly x 4, then q2 weeks; Cis-Platinum day 1, day 36, then q2 weeks VERSUS 2. Cyclophosphamide, Adriamycin, Cis-Platinum q4 weeks.
	NCIC BR.6*	To compare early versus late radiotherapy in limited small cell carcinoma for patients being treated with Cyclophosphamide i.v., Adriamycin i.v., Vincristine i.v., cycles 1, 3, 5 alternating with VP-16 i.v., Cis-Platinum i.v. daily x 3 days cycles 2, 4, 6.

	NCIC IND.7	To determine the response and toxicity of mesothelioma of lung to mitoxantrone.
Lymphoma	NCIC LY.3	Comparison of Standard BACOP chemotherapy with Escalated BACOP in "poor prognosis" histology.
	NCIC IND.16	To investigate the effectiveness of Acivicin (AT-125) in patients with poor prognosis, Non-Hodgkin's lymphoma in whom conventional treatment(s) are ineffective.
	M.NHL.85.5	To compare efficacy, toxicity and evaluate quality of life between Cyclophosphamide, Vincristine, Prednisone and Epirubicin, Vincristine, Prednisone in the treatment of favourable histology Non-Hodgkin's Lymphoma Stage IIB, III A & B, and IV A & B.
Hairy-Cell Leukemia	NCIC IND.22	To determine the response and toxicity of hairy cell leukemia to 2'-Deoxycoformycin (DCF) given in a low dose intermittent schedule.
Hodgkin's Disease	NCIC HD.4	To study the effectiveness of MOPP/ABV Hybrid chemotherapy versus alternating MOPP/ ABVD for remission induction, durability and survival in advanced or recurrent disease.
Chronic Lymphatic Leukemia	M.CLL.82.1	To determine the response rate of patients with refractory CLL to weekly doses of 2'-Deoxycoformycin (Phase II).
Multiple Myeloma	NCIC MY.3	Pilot study of weekly CTX and Prednisone for patients unresponsive to Melphalan and Prednisone therapy.
	N.MY.84.1	Pilot study of weekly cyclophosphamide and alternate day Prednisone therapy (CWAP) as primary treatment in multiple myeloma, stages 1 to 4.
Malignant Melanoma	NCIC ME.5	Surgical study to determine the safest excision margins around the primary melanoma and to evaluate the management of the regional lymph nodes. A national intergroup protocol.
	NCIC IND.14	To determine the efficacy of N-Methylformamide in malignant melanoma.
Colorectal Carcinoma	NSABP C-02	To evalute postoperative portal vein infusion of 5-FU in resectable adenocarcinoma of colon.

	NCIC IND.8	To determine the efficacy of N-Methylformamide in patients with colorectal carcinoma.
	M.CR.84.2	To determine efficacy of Methotrexate and 5-FU (with leukovorin rescue) in patients with advanced colon or rectal carcinoma.
	M.CR.85.9	To determine the efficacy and toxicity of Methotrexate and 5-FU (with leukovorin rescue) in patients with advanced colon or rectal carcinoma.
Rectal Carcinoma	NSABP R-01	To compare no treatment versus combination chemotherapy versus radiotherapy in patients with Duke's B or C rectal carcinoma after surgery.
Breast Carcinoma	NCIC MA.4	To compare Tamoxifen versus Tamoxifen plus combination chemotherapy in patients with ER or PR positive stage II breast carcinoma. To compare no treatment versus combination chemotherapy in patients with ER and PR negative stage II breast carcinoma.
	NSABP B-13	To compare no treatment versus combination chemotherapy in patients with ER and PR negative stage I breast carcinoma.
	NSABP B-14	To compare placebo versus Tamoxifen in patients with ER or PR positive stage I breast carcinoma.
	NSABP B-15	To compare Adriamycin plus Cyclophosphamide versus Cyclophosphamide plus Methotrexate plus 5-FU versus both regimens sequentially in patients with PR negative stage II breast carcinoma.
	NSABP B-16	To compare no chemotherapy versus Adriamycin plus Cyclophosphamide versus Melphalan plus 5-FU in patients with PR positive stage II breast carcinoma.
Gastric Carcinoma	M-GA.85.4	To compare efficacy and evaluate quality of life of Epirubicin plus 5-Fluorouracil vs. 5-FU alone vs. Epirubicin alone in the treatment of locally advanced or disseminated gastric cancer.
Prostate Carcinoma	M.PR.84.5	To compare the effectiveness of megastrol acetate plus Diethylstilbestrol (DES) to DES in Stage D2 prostate cancer.
	M.PR.84.6	To compare orchiectomy and antiandrogen (Flutamide) vs. LHRH agonist and antiandrogen (Flutamide) for efficacy and toxicity in newly diagnosed Stage D2 prostate cancer.

	M.PR.85.2	To assess the effectiveness of the antiandrogen (RU-23908) and orchiectomy by comparing orchiectomy and placebo in Stage D2 prostate cancer.
	M.PR.85.3	To compare the efficacy and toxicity of ketoconazole vs. diethylstilbestrol in the treatment of Stage D prostate cancer.
Laryngeal Carcinoma	M.H&N.82.1	To compare radiotherapy versus radiotherapy plus combination chemotherapy in patients with advanced carcinoma of larynx or hypopharynx without distant metastases.
Head & Neck Carcinoma	M.H&N.84.3	To determine efficacy of high dose Methotrexate plus PaLa chemotherapy in patients with advanced head and neck carcinoma.
Sarcoma	M.SA.80.1	To determine whether Metronidazole is synergistic with Adriamycin in patients with advanced soft tissue sarcoma.
Supportive Care Protocols	NCIC IC.4	To assess the role of the antibiotic azthreonam and to determine the optimum duration of therapy in responding patients in febrile patients with neutropenia secondary to chemotherapy.
	M.SC.84.4	To determine the effectiveness of Droperidol in patients with persistent chemotherapy related nausea and vomiting.
	M.SC.83.9	To compare sustained release morphine tablets versus oral morphine liquid in cancer analgesia.
	M.SC.85.7	To determine the effectiveness of piroxicam added to morphine as an analgesic in cancer patients.

MEDICAL ONCOLOGY NURSING

Medical Oncology Nursing at the Foundation is ably led by Nancy Johnson in the Chemotherapy Clinic with a staff of five chemotherapy nurses and four nursing aides devoted to the education, support, and particularly expert administration of parenteral chemotherapy for their patients and by Janice Lutz, Protocol Nurse Co-ordinator and Protocol Nurse Kerry McDonald in the Clinical Investigation Office.

Medical Oncology Nurses participate in Respiratory Rounds with the staff at the Respiratory Centre to improve follow-up care of lung cancer patients. Similarily, regular Nursing Conjoint Rounds with Social Service have been beneficial in identifying high risk situations

and intervening with appropriate measures to prevent crisis development. Increasing awareness of the role of the Oncology nurse by the University of Manitoba and Health Sciences Centre Schools of Nursing has been evidenced by placement of senior nursing students at the Foundation as part of their clinical experience. Education in the wider community continues to be encouraged and medical oncology nurses lecture programmes continue to attract nursing attendance from throughout the province. The nursing staff also frequently act as guest speakers at other urban and rural health institutions. Continued participation in national and international oncology meetings enhances skillful evaluation and counselling for patients and their families.

Our two nurse oncologists who completed the Faculty of Medicine second year undergraduate programme in physical diagnosis previously are proficient in assisting medical oncologists in clinical evaluation of patients at the Oncology Centre, and in addition provide a critical liaison between patient care in the clinic and clinical investigation (protocol) activities including evaluation of patients with respect to eligibility, informed consent, and on-going assessment during therapeutic trials. Nursing research is fostered in conjunction with the University of Manitoba School of Nursing and with National Cancer Institute, National Surgical Adjuvant Breast and Bowel Programme, as well as institutional protocols.

Medical Oncology clinics are actively cooperating with Professor Lesley Degner and Karen Neufeld, R.N., in nursing research projects in patients' desire for control preferences and measuring desire for control in health practises.

Nursing members are actively participating on a provincial committee with the Manitoba Association of Registered Nurses in developing comprehensive standards for the emerging specialty of Oncology Nursing. During 1985, approval and funding was secured from the Manitoba Health Services Commission for installation of laminar flow drug preparation cabinet.

PATIENT CARE

Optimal patient care is in the primary objective of the Department of Medical Oncology. The Medical Oncology Clinic, in conjunction with the unit at St. Boniface Hospital, serves as the Manitoba referral centre for care of patients with neoplastic and hematologic diseases. The adult clinic also operates in close co-operation with active pediatric oncology clinics, which are reported in detail elsewhere in this Report. While the clinic itself is strictly an ambulatory (outpatient) facility, all attending oncologists hold major University of Manitoba appointments and are on active staff at the contiguously adjacent General Centre of the Health Sciences Centre. Accordingly patients requiring admission to Hospital are admitted to the General Centre where they are attended in continuity by their medical oncologist.

During 1985, Doctor Lynn Pratt, family physician, joined the Foundation on a part-time basis, and is ably assisting the medical oncologists in clinic.

Further to repeated requests by the Foundation, the Health Sciences (General Centre) is developing a proposal to commit a 19 bed ward (D-6) as an interim, geographic oncology clinical teaching in-patient unit.

Table II illustrates the ambulatory (out-patient) services: (See also separate report for St. Boniface Hospital Unit).

TABLE II
MEDICAL ONCOLOGY PATIENT STATISTICS#

	New Patients#	Follow-up Visit	Total Physician Clinic Visits	Number of Treatment Courses
1980*	365	5049	5414	1976
1981*	554	6894	7448	2619
1982*	620	8249	8869	3885
1983	293	5107	5400	3269
1984	287	5125	5412	3584
1985	291	5313	5604	3717

*Figures for the years 1980-1982 include St. Boniface General Hospital medical oncology patients, plus MCTRF gynaecological, surgical, and urological clinics. Since 1982, these patient statistics are presented in their respective sections of the Report.

#These figures do not include approximately 400 consultations provided by Department members to in-patients located at the Health Sciences (General Centre).

PUBLICATIONS*

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Johnston, J. B., Begleiter, A., Pugh, L., Leith, M., Wilkins, J. A., Cavers, D. J., and Israels, L. G.: The biochemical changes induced in hairy-cell leukemia by the adenosine deaminase inhibitor 2'-deoxycoformycin. Cancer Res. (in press).

Johnston, J. B., Eisenhauer, E., Barr, R., Feldman, L., Maksymiuk, A., Scott, G., Sutton, D., Venner, P., and Walde, D.: 2'-Deoxycoformycin (DCF) in hairy-cell leukemia (HCL): A Canadian Phase II trial. (submitted for presentation).

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Riddell, Johnston, J. B., Rayner, H. L., and Israels, L. G.: Response of Waldenstrom's macroglobulinemia to 2'-deoxycoformycin. Cancer Treat. Rep. (in press).

Schipper, H., Levitt, M.: Measuring Quality of Life: Risks and Benefits. Cancer Treat. Rep., 69, No. 10, Oct., 1985.

*Publications of clinical impact are listed. Publications related to basic research — see "Cell Biology Institute" report.

PEDIATRIC ONCOLOGY

Section Head — J. M. Gerrard, M.D., Ph.D., F.R.C.P.(C)
A. J. Bishop, B.Sc., M.D., F.R.C.P.(C)
E. D. Israels, B.A., M.D., M.Sc.
S. J. Israels, M.D., F.R.C.P.(C)
N. L. Kobrinsky, B.Sc.(Med.), M.D., F.A.A.P., F.R.C.P.(C)
M. L. Schroeder, M.D., F.R.C.P.(C)

ONCOLOGY NURSE

P. Pruden, R.N.

HOME CARE CO-ORDINATOR

K. McRae, R.N.

SOCIAL WORKER

S. Powell, B.S.W.

PSYCHOLOGIST S. Goszer-Tritt, Ph.D., M.A., B.A.

PLAY CO-ORDINATOR

W. Leslie, J. Dewar

TEACHER

J. Wright, B.A., B.Ed.

DATA MANAGERS

L. Janke, M.R.T., H. Kampen, M.R.T., K. Hjalmarsson, M.R.T.

CHAPLAIN

A. Goodwin, B.Sc.N., M.Div.

RESIDENTS

B. Chan, G. Kimmons, E. Enns

SUPPORT STAFF

L. Devlin, J. Powell

PATIENT CARE

The Pediatric Section is a primary referral centre for children with oncological diseases for the Province of Manitoba and has developed a comprehensive care program for pediatric patients with cancer. Out-patient services are coordinated through the Cancer Foundation and in-patient care is co-ordinated through the Children's Hospital. A treatment team including a pediatric oncologist, a social worker, oncology nurse, homecare co-ordinator, play therapist, teacher and chaplain are responsible for directing the treatment program of the individual patient whether the care setting is out-patient, in-patient or home.

The oncology nurse, Pat Pruden, plays a major role not only in the administration of chemotherapy, but also in the education of the patient and his or her family, friends and school with regard to the illness, therapy and complications of therapy. She also provides inservice educational sessions for paramedical personnel who participate in the care of the child with cancer, and co-ordinates weekly meetings of the entire treatment team. In addition, Pat made presentations to the Manitoba Neurology Nurses, the Canadian University Nurses Association and the Canadian Cancer Society Annual Meeting in Brandon.

The psychosocial support services continue to be provided by one social worker, Susan Powell, from the Children's Hospital. The service fully recognizes that a life-threatening illness in a child has major implications for the entire family. Every family has an opportunity to meet with the social worker, and if the need arises, counselling services are provided for the patient and other members of the family. Crisis prevention is an important aspect of this support service. The social worker provides an essential liaison role with the Children's Hospital in community resources to assist families with practical and emotional support. She assists in organizing information meetings for new families to familiarize them with the clinic and staff. Susan Powell has also been helpful in the establishment of a self-help group for teenagers with cancer, and provides support and information to the parent self-help group, "Jeffrey's Folks" which provides one-to-one support for any parent of a child newly diagnosed with cancer who would like to meet and talk with another parent who has experienced having a child with cancer. The teen group met every two weeks and was generally well attended by children on and off treatment. A summer barbecue and Christmas party were also held. The parents' support group, Jeffrey's Folks, was officially established as a satellite group of the Service-to-Patients Committee of the Canadian Cancer Society. This allows financial independence and a wider access to the public. In October, Pat Pruden met with their board members to discuss their plans for the future year. At their monthly meetings, they have guest speakers addressing varied subjects, such as AIDS, chronic illness and the effects on the family. In June, 1985, through the generosity of the Canadian Cancer Society, a week-end camp was held for the patients and their siblings at Arnes, Manitoba. This camp was unique in that there were scheduled workshops to explore emotions of both patients and siblings. The week-end was a great success, and the Canadian Cancer Society has kindly agreed to undertake sponsorship of such a camp for the next five years. A major presentation highlighting the camp's success will be given at the annual Association for the Care of Children's Health Conference being held in San Francisco in June, 1986.

Play therapy, under the direction of the Child Life Section of the Children's Hospital, continues to be an extremely important aspect of the young patient's visits to the Foundation Clinic. This program reduces the anxiety of both patient and parents and also allows siblings to participate in the activities of the clinic. Through play and our highly sophisticated puppets specifically designed to demonstrate such common procedures as intravenous therapies, punctures, marrow aspirations, surgical procedures and complications of therapy, this program greatly enhances the young child's understanding of his or her illness. In addition, the play therapy program allows the therapy team to augment our knowledge of the patient's response to the disease or the treatment, since the young child frequently tells us more through play than through verbalizing.

The need to provide a wide range of educational services for students receiving treatment at the Cancer Foundation has been recognized for some years. Joyce Wright continues to

effectively fill this position and to develop a model based on service needs and demands. Children who are under the care of the Cancer Foundation are strongly encouraged to carry out as normal a lifestyle as possible, including regular school attendance. On occasion due to distance from home or to the complexity of the treatment program this is not possible. Children are then kept current in their school program either by provision of one-on-one tutoring by the oncology teacher or where it is appropriate to involve the child in a classroom setting (especially the young child who needs group activities), the child is introduced into the class at the Children's Hospital. The teacher maintains an on-going liaison with the home school, and in addition, visits the patient's school often with the oncology nurse and social worker. The objective of these visits is to help both teachers and classmates understand and be more comfortable with the child with cancer. Each visit is designed to meet the needs of a particular situation. The home school may draw upon administration, resource teachers, guidance personnel and special education co-ordinators. We are grateful to the Canadian Cancer Society for providing the funds for the travel required to the rural schools.

The oncology teacher, nurse and social worker will also visit, if requested, classrooms of children who have cancer or who have died of cancer to discuss various aspects of cancer with the students and teachers. As part of this program, entire classes have visited the clinic area. The young students learn a great deal and are sensitized in a non-threatening manner. They have the opportunity to view an examination room, medical instruments and equipment and receive an explanation or demonstration of procedures. Members of the class gain an understanding of the clinic environment and an appreciation of what the classmate, the patient, experiences. The patient benefits greatly from the increased understanding of his classmates. For both, much of the mystique and fear has vanished. Very positive feedback has occurred from these field trips. Teachers have commented on how easily the children were able to discuss cancer. This program also fulfills the important role of the Foundation in educating the public. With the co-operation of the Cancer Foundation, the Children's Hospital of Winnipeg and the Winnipeg School Division No. 1, workshops for teachers in the province who have children with cancer in their classrooms, are now an annual event. The Section appreciates the response received from the provincial department of education, in particular Winnipeg School Division No. 1, in seeking methods and resources for meeting these needs. In 1985, this program was highly successful with 41 meetings with teachers, 8 class meetings and 4 classroom tours of our premises. In addition, a one day conference was held in November for educators dealing with children with cancer.

We continue to be grateful for the support services given to the staff, patients and their families by the chaplaincy of Reverend Ann Goodwin. The role of hospital chaplains in the pediatric oncology program is also one which is challenging and one from which we are gaining an understanding of the spiritual needs of children.

Ronald McDonald House, a facility which provides "a home away from home" for the rural families undergoing therapy in Winnipeg, was opened in the spring of 1984 and continues to play a very important role in 1985. The many parents, patients, members of the therapy team and administration representatives of the Children's Hospital who gave much time and energy in the establishment of this House, continue to play a large role in its maintenance. This facility has enriched our program and has added greatly to the support system of our rural patients.

The Section of pediatric oncology is part of the Children's Cancer Study Group, a group comprised of people from institutions at the forefront of the treatment of cancer throughout North America. As part of our involvement with the Children's Cancer Study Group, we participate in treatment protocols and studies which have been very carefully designed to provide cancer patients in Manitoba with the most up-to-date treatment. At the same time this program allows the introduction of new treatment programs in such a way that we can carefully evaluate them. Programs such as these with the Children's Cancer Study Group have been largely responsible for the improvement of a number of childhood cancers. Particularly remarkable has been the gradual improvement of children with some forms of acute lymphocytic leukemia (ALL) who can now be cured in about 8 out of 10 cases. Significant but less dramatic progress has been made in many other forms of childhood cancer, and we hope through this and other programs to continue this improvement.

Full support is available from the Department of Pediatrics, University of Manitoba in essential sub-specialties such as immunology, allergy, infectious disease, neurology, genetics, endocrinology, surgical sub-specialties, metabolism, nutrition and child development.

The Section is grateful for the support and co-operation of the Administration of the Foundation, the Children's Hospital and Winnipeg School Division No. 1, in allowing personnel to cross institutional, geographical and functional boundaries, since, without this support, true comprehensive care for the pediatric oncology patient would not be possible. The Section also is grateful to the Canadian Cancer Society for the assistance which it has given us in the development of many of our support programs.

Out-Patient Statistics, 1985

New Patients	204
Follow-up	1,889
	2,093
Procedures:	
Physician	216
Nursing:	
Chemotherapy	1,286

EDUCATION

The Section is fully approved for sub-specialty training by the Royal College of Physicians and Surgeons of Canada, and as a Section of the Department of Pediatrics, University of Manitoba, the teaching and educational programs of the Foundation for medical personnel include:

(a) Training of career pediatric oncologists/hematologists in order to permit them to pick up academic positions and assume careers of clinical practice, teaching and research. All candidates must conform to university entrance requirements for post graduate medical trainees and must have completed their core general pediatric training.

(b) The exposure of other oncology trainees (internal medicine, surgery) to the pediatric oncology patient.

(c) The provision for general pediatric residents of sufficient and appropriate exposure to modern hematology and oncology.

(d) The training of basic scientists in research encompassed within the discipline of pediatric hematology/oncology.

The Pediatric Section also participates in a formal elective program for students from the University of Manitoba School of Nursing.

The participation of the nurse, social worker, teachers, play co-ordinator and parents in education of their colleagues, the patients and their families has been discussed previously.

RESEARCH

The Section actively supports clinical investigation aimed at current clinical problems in pediatric hematology/oncology and in the development of long term basic research. Just over $450,000 in grant and external funds was received by the various Section members for studies in 1985.

On-going clinical investigation and basic research in which the Section is participating at the present time:

1. Children's Cancer Study Group: Affiliated member since 1978. All new patients are registered with CCSG and approximately 85% of patients are on study protocols. A. J. Bishop, N. Kobrinsky, S. Israels, M. Schroeder.
2. Research, education and patient care within a Hemophilia Agency. N. Kobrinsky. (Manitoba Chapter of the Canadian Hemophilia Society).
3. The antenatal treatment of erythroblastosis fetalis by maternal administration of high dose intravenous gamma globulin. N Kobrinsky, J. Bowman, A. J. Bishop (Children's Hospital Research Foundation and the Manitoba Medical Services Foundation).
4. The role of DDAVP in the treatment of dysfunctional platelet syndromes, von Willebrand disease and bleeding problems. N. Kobrinsky, J. Gerrard, S. Israels, A. Bishop.
5. The development and evaluation of reentry programs for children with cancer. Joyce Wright.
6. HLA and disease. M. Schroeder.
7. Studies of platelets, coagulation proteins and bleeding disorders. J. Gerrard, E. Israels, S. Israels (Children's Hospital Research Foundation, Medical Research Council).
8. The balance of thromboxane and prostacyclin in cardiovascular disease. J. Gerrard (Canadian Heart Foundation).
9. Basic studies of platelets, natural killer cells and malignancies. J. Gerrard (National Cancer Institute and the Medical Research Council of Canada).
10. Platelet allo-immunization: A comparative study of two techniques. M. Schroeder (Manitoba Medical Services Foundation).
11. Platelet associated IgG — its relationship with thrombocytopenia in the neonate. M. Schroeder (Canadian Red Cross Transfusion Service).

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Kobrinsky, N. L., McAngus, N. J. Endothelial cells suppress granulopoietic clusters and stimulate large GM-CFUs in culture. J. Clin. Invest.-Med. 8(2):160-166, 1985.

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GYNECOLOGIC ONCOLOGY

SECTION HEAD:

Garry V. Krepart, M.D., B.Sc.(Med.), F.R.C.S.(C), F.A.C.O.G.

SECTION MEMBER:

Robert J. Lotocki, M.D., B.Sc. F.R.C.S.(C)

CLINICAL FELLOWS:

Dr. John F. Jeffrey, M.D., F.R.C.S.(C)
Dr. Jill Nation, M.D., B.Sc.(Med.), F.R.C.S.(C)
Dr. John Mazurka, M.D., F.R.C.S.(C)

RESIDENTS:

Dr. C. Collister, Dr. M. Bernier, Dr. J. Johnson, Dr. G. Bourgeois-Law, Dr. G. Ryan, Dr. M. Helewa

NURSING STAFF:

I. Chrunyk, B. Lucko

NURSING AIDES:

I. DeSousa, L. Jonasson, G. Harvey

SECTION OF GYNECOLOGIC ONCOLOGY

ORGANIZATION

The Section of Gynecologic Oncology is represented at the Manitoba Cancer Treatment & Research Foundation as well as at the St. Boniface Oncology Unit at the Health Sciences Centre and St. Boniface General Hospital. Members belong to the Section of Gynecologic Oncology of the Department of Obstetrics, Gynecology & Reproductive Sciences of the Faculty of Medicine. Clinics are held four one-half days weekly at the Manitoba Cancer Treatment and Research Foundation and three one-half days at the St. Boniface Oncology Unit. Close liaison is maintained with the Radiotherapy and Medical Oncology Divisions as well as urologic and surgical oncologists at both institutions. Referred patients are seen at both Oncology units and appropriate consultations, if needed, are made with other divisions. Hospital admissions are at the Women's Hospital or at St. Boniface Hospital. An Oncology Unit as well as a high-dependency area and a dedicated in-patient chemotherapy nurse is available at the Women's Hospital with similar facilities at St. Boniface Hospital on the Gynecology Service.

TEACHING

Various levels of teaching are offered by the Gynecologic Oncology Service. A two-year postgraduate Fellowship Program was established in 1981. Currently the Program has two Fellows, one in each year of fellowship, with new Fellows already accepted for 1985-87. Dr.

John Jeffrey finished in July of last year and has accepted a position in the Section of Gynecologic Oncology, Department of Obstetrics & Gynecology at Dalhousie University. Dr. Jill Nation also finished in 1986 and will join the Section of Gynecologic Oncology at the University of Calgary. Dr. John Mazurka entered a two year Fellowship in July, 1985.

Residents in their third and fourth year rotate through the Section for three month rotations as part of their training in the Department of Obstetrics, Gynecology & Reproductive Sciences. Tumor Conferences are held weekly at the Women's Hospital and St. Boniface Hospital with much appreciated pathology backup by Dr. M. Paraskevas and by Dr. G. Vadas. Reviews of current subjects in Gynecologic Oncology or pertinent clinical cases are presented for all residents, medical students, interns and staff.

The Section is responsible for chemotherapy as well as surgery. Bowel as well as urinary complications as they relate to gynecologic malignancy or its treatment complications are handled at both teaching hospitals. Full support is available from all subspeciality areas, including T.P.N., infectious disease, surgery, urology and physiotherapy. Full access to medical workers, chaplaincy service, pharmacy, occupational therapy and dietetics is available and a weekly nursing conference with all support staff represented is held. Slightly less than 1,000 in-patients were admitted in 1984 at both the Women's Hospital and St. Boniface Hospital units.

CLINICAL INVESTIGATION

The Section is active in the N.C.I.C. Ovarian Cancer Protocols, both at the level of the writing committee and patient treatment. Currently patients with ovarian cancer are entered into OV6, OV7 or OV8 protocols.

Other interests of the Section include:

a) Surgical staging of endometrial carcinoma with an eight year review of the Manitoba Cancer Treatment & Research Foundation's experience.

b) Place of second look laparotomy in cancer of the ovary.

c) Chemotherapy treatment of ovarian sarcomas.

d) Frequency of cervical cytology.

e) Colposcopy in preinvasive cervical lesions and the use of laser in cervical, vaginal and vulvar preinvasive disease.

f) The role of staging laparotomy in early ovarian cancer.

g) The role of chemotherapy in ovarian carcinoma of low malignant potential.

SECTION OF GYNECOLOGIC ONCOLOGY STATISTICS

Manitoba Cancer Treatment & Research Foundation and St. Boniface Oncology Clinic

	New Patients	Follow-up Visits	Total Patient Visits
1984	314	3,810	4,189
1985	423	3,781	4,204

Colposcopy (St. Boniface)

	New Patients	Follow-up Visits	Total Patient Visits
1984	275	808	1,083
1985	413	1,126	1,539

Hospital Admissions — 1984

	Health Sciences Centre	St. Boniface General Hospital	Total
Surgical	307	115	422
Non-surgical	480	75	555
Total	**787**	**190**	**1,007**

PUBLICATIONS

Ovarian Carcinoma 1985. The Continuing Challenge. A Symposium — Contemporary OB-GYN, August, 1985.

PRESENTATIONS

"Chemotherapy During Pregnancy" — Society of Obstetricians and Gynecologists of Canada Postgraduate Course. Barbados, February, 1985, G. V. Krepart.

"New Perspectives in Ovarian Cancer" and "Hormonal Replacement Therapy". Gynecological Surgery and Oncology Symposium. Tom Baker Cancer Centre, Calgary, Alberta, March 21-22, 1985, G. V. Krepart.

"Second Look Laparotomy in Ovarian Cancer" Felix Rutledge Society, Graz Austria, May, 1985, G. V. Krepart.

"Staging Inaccuracies in Stage I Carcinoma of the Endometrium". Society of Obstetricians & Gynecologists of Canada Annual Meeting. Jasper, Alberta, June, 1985, G. V. Krepart.

"Staging Laparotomy in Early Ovarian Carcinoma". Society of Obstetricians & Gynecologists of Canada Annual Meeting, Japser, Alberta, June, 1985, M. Helewa.

"Borderline Ovarian Carcinoma", Society of Obstetricians and Gynecologists of Canada Annual Meeting, Jasper, Alberta, 1985, J. Nation.

"Epidemiology of Cervical Cancer", Canadian Society of Laboratory Technicians, Winnipeg, Manitoba, June, 1985, G. V. Krepart.

"Clinical Laboratory Diagnosis of Ovarian Cancer" and "Surgery and Chemotherapy of Ovarian Cancer", Florida Osteopathic Medical Association Midyear Seminar, Clearwater, Florida, October, 1985, G. V. Krepart.

ONCOLOGY UNIT
St. Boniface General Hospital

Oncology Services Director — Dr. B. H. Weinerman, M.D., F.R.C.P.(C)

Head Nurse — A. Meekison, R.N.

RADIATION ONCOLOGY

Radiation Technologists — G. Ogilvie, R.N., R.T.T., Supervisor;
S. Hutton, R.N., R.T.T.; S. Sharpe, R.T. (R); B. Dodds, R.N., R.T.T.
Clinic Nurse — B. Lucko, R.N.; R. Olson, R.N., R.T.T.

MEDICAL ONCOLOGY

Director — B. H. Weinerman, M.D., F.R.C.P.(C)
H. Schipper, B.Sc., M.D., F.R.C.P.(C)
E. J. Bow, M.D., MSc., D.BACT, F.R.C.P.(C)
A. M. Shojania, M.D., F.R.C.P.(C)
J. Foerster, B.Sc.(Med.), M.D., F.R.C.P.(C)

Nursing Staff — B. Scott, R.N. — Assistant Head Nurse,
A. Acheson, R.N.; D. Self, R.N.; I. Lemoine, R.N.

Nurse-Practitioner — E. Bebchuk, R.N.

Secretarial Staff — P. Rubel, D. Firth, B. Scott.

Support Staff — C. Berthelette, Senior Ward Clerk
R. Provitina, Ward Clerk
H. Lucy, Orderly
E. Denewith, Nurse's Aid

Protocols — E. Stiles, Protocol Data Manager

OUTREACH

Director — H. Schipper, B.Sc., M.D., F.R.C.P.(C)
Coordinator — V. Mann, R.N., B.A.; A. Nemecec, R.N.
Secretary — D. Firth

SOCIAL WORK

J. Taylor-Brown, BSW.

PHARMACY

D. Dickoff, B.Sc. Pharm.

ONCOLOGY UNIT — ST. BONIFACE GENERAL HOSPITAL

The St. Boniface Hospital Oncology Unit is a fully integrated joint program of the Manitoba Cancer Treatment and Research Foundation and the St. Boniface General Hospital. The original unit, a radiation oncology program, in the St. Boniface General Hospital under the guidance of senior radiotherapist, Dr. James Bennett, provided radiation therapy services to referred patients for thirty years. Presently, a team of radiotherapy oncologists from the Manitoba Cancer Centre rotate through St. Boniface providing the radiotherapy consultation and expertise.

In 1973, with the introduction of a formal chemotherapy program at the hospital, and with the subsequent growth of that program, a different cooperative effort between the St. Boniface Hospital and the Foundation began to evolve. This arose because of the increased demands for chemotherapy. In 1975, a joint program established an outpatient oncology clinic in the ambulatory care facility of the hospital.

A New Outpatient Facility

The eventual need for expanded outpatient facilities brought on by the enlarging patient population and the requirement for a new cobalt unit resulted in the planning of a new outpatient oncology facility which had its sod turning ceremony in July of 1982. The new facility had its official opening April 1984. The new six million dollar wing of St. Boniface General Hospital became the site of a modern cancer diagnostic and treatment centre. The three-storey annex is adjacent to the x-ray department and thereby places the cancer diagnostic and treatment facility adjacent to radiological and ultrasound facilities. This facility increases the efficiency of the two oncology areas by physically joining them and thereby better utilizing nursing and other support personnel. A joint nursing coordinator, Mrs. B. Glenday, was appointed. Ms. A. Meekison was subsequently appointed when Mrs. Glenday became Director of Nursing for the Foundation. This position serves to cement the entire oncology area and also adds a link to the inpatient oncology unit. This latter unit was opened in September 1984 as a forerunner to a more expanded unit including gynecological oncology. The new unit emphasizes a pleasant atmosphere for patients with pleasant working conditions and increased efficiency for the staff.

In 1983 due to the growing complexity of radiotherapy planning and treatment, the radiotherapists began a rotation to St. Boniface Hospital from the Foundation to better serve patients with the advanced facilities present at the Foundation. The new cobalt unit installed with the building allows a broader range of patients to be treated within this unit.

Teaching

The oncology program is fully integrated with the University and the Foundation in the instruction of undergraduate students and post-graduate interns and residents. As well as individual instruction, residents and fellows take part in the consultation and outpatient rotations. Twice weekly walk rounds with all the medical oncology staff serves as an ongoing audit of patient care, as well as an ongoing discussion of all interesting and difficult hospital patients. Dr. M. Shojania, Director of the Haematology Laboratory at St. Boniface Hospital takes a full participatory role in all teaching and round programs. Drs. I. Carr, and L. Lu of the Department of Pathology participate in one of the weekly rounds.

Research

Local, Canadian and International trials are running in the unit with the medical staff participating in and drawing up many of the protocols. In 1985 263 new patients were enrolled in investigational protocols with 186 patients on study and a total of 226 patients being actively followed. Examples of this research are areas of infections in granulocytopenic patients with Dr. Bow, new drugs with Dr. Weinerman, outreach, Dr. Schipper and support services to patients (John Farber). Some of the specific research programs are listed below.

- Biochemical modulation of 5-Fluorouracil with methotrexate in patients with metastatic colorectal cancer.
- A trial of systemic chemotherapy with 5 FU and Methotrexate in mice bearing dimethylhydrazine induced colon cancer.
- New investigational drug trials.
- Colon cancer research group to examine pathology and treatment of colon cancer.
- Acute leukemia research group for the formalization of treatment protocols for acute leukemia.
- Central venous catheter placement study for immunocompromized patients.
- Subcutaneous port program with programable pumps to look at out-patient infusion chemotherapy.
- Herpes simplex oesophagitis in immunocompromized patients with cancer.
- Electronic diaphanography.
- Quality of life studies in cancer patients.
- Further development of the Outreach Program.
- Study of coagulopathy following peritoneo-venous shunt.
- The effect of thiazine dyes in coagulation and immunological reactions.

OUTREACH PROGRAM

This program is operated by the Foundation from the St. Boniface Hospital. It is designed to develop safe methodologies for effective chemotherapy administration in rural areas of the province. Specific areas of research development include information handling and transmission techniques for computerized record maintenance from a central facility to the outreach centres. The program has already developed and validated a quality of life index and compared the treatment of breast cancer in the urban and rural populations.

ONCOLOGY NURSING

I. Patient Care

The reason d'etre of the unit is the service to patient. St. Boniface Hospital serves as a tertiary referral centre in Manitoba for the treatment of cancer patients. In 1985 our unit saw 492 new patients (100 more than the year before). Very quickly our new area is being stretched to its capacity. The unit has utilized a highly developed infrastructure involving nursing, social work, pharmacy, home care, and the hospital ward to maximize patient support.

II. Patient Activities

This year showed a marked increase in nursing procedures. This is in part due to the physical increase in space which the new area provided, thus allowing an increase in services provided to patients.

a) Eight patients can now be accommodated in the treatment area at one time.

b) Blood and blood component therapy can now be administered on an out-patient basis.

c) Certain chemotherapy treatments previously requiring admission, can be administered in the treatment room as the in-hospital bed situation or patient preference demands.

III. Practice Activities

1. Three nurses from 5B-Medicine and two nurses from 3B-Gynecology designated to administer chemotherapy on those wards attended the theory presentation of the Oncology Nursing Workshop and received their clinical practicum in the St. Boniface Unit. This occurred in conjunction with the opening of the in-hospital chemotherapy beds on 5B-Medicine and the increased chemotherapy workload on 3B-Gynecology secondary to an increasing patient population.
2. A multidisciplinary panel discussion was presented at Nursing Excellence Day in April. In cooperation with 5B-Medicine, Social Service and Home Care, the complex care requirements of the leukemic patient were addressed.
3. In cooperation with Dianna Dickof, Special Services Pharmacist, procedures for general maintenance, drug preparation and cleaning of the Vertical Laminar Airflow Hood was established.
4. Weekly Home Care Rounds have been initiated with Radiotherapy at which time patients are identified who require the services of Home Care and/or 3E Palliative Care.
5. In-hospital chemotherapy treatments for the gynecology patients on 3B is coordinated by Bernice Lucko, Radiotherapy clinic nurse. This provides excellent continuity of care between the two areas.
6. In November, an Outpatient Oncology Information Day was piloted involving the many disciplines which comprise our unit. Response was very favourable and plans are in progress to provide the inservice day on an ongoing basis to health care professionals within the hospital and the community.

SOCIAL WORK

Summary of Social Work Activity in Oncology at St. Boniface Hospital.

Year	New Files Opened	Avg. Number opened/mo	Avg. Monthly Caseload	Service hrs. to pt.	Service hrs to prog.*
1984 (Apr-Dec)	43	4.8	65	685	313
1985	97	8.1	78.2	1146	344
% change	+69.1**	+68.8	+20.3	+25.5**	-17.6**

*Includes research, rounds, inservice, planning, etc.
**1984 Pro-rated over 12 months to calculate % change.

Patient Care

The year 1985 marked the first complete year that Social Work had an approved full-time Social Worker in the Oncology Program. The Table above summarizes Social Work activity in Oncology for 1984 and 1985. Dramatic increases were experienced in both the number of patients seen (files opened and caseload average) and the service provided to patients and families (service hrs. to patients).

This year saw continued involvement in training of Cansurmount volunteers. The patient handbook initiated in 1984, was completed in 1985 and will be going to press in early 1986.

The relaxation therapy program initiated in 1984, continued in 1985.

Education and Research

The Department of Social Work continued its participation in educational and research programs during 1985. Social Work staff again contributed to the training of oncology nurses through the Outreach Program, Chemotherapy Orientation Project. The volume entitled the Psychosocial Impact of Chemotherapy on Patients and Families, used in conjunction with out presentation, was revised in 1985 and will be reprinted in 1986.

Social Work, along with colleagues from Ontario, Alberta and British Columbia, participated in the planning of the first Canadian Psychosocial Oncology Conference. The Department was also an active collaborator in 1985 in the creation of a Canadian association of psychosocial oncology.

TABLE I — Medical Oncology Statistics, St. Boniface General Hospital

	New Patients	Follow-up visits to doctor	Total Physician Visits	No. of Patient Treatments	Procedures
1981	224	2,242	2,466	2,326	N.R.
1982	306	2,580	2,886	2,152	N.R.
1983	377	4,257	4,694	3,753	3,399
1984	395	4,141	4,536	2,699	4,984
1985	492	4,656	5,148	2,475	9,483

TABLE II — Protocol Statistics, St. Boniface General Hospital — 1985

GROUP	On Study 1984	On Study 1985	New Patients Entered (1984)	New Patients Entered (1985)	Off Study During 1985	Patients on Active follow-up 1984	Patients on Active follow-up 1985
NCIC	59	63	16	28	9	63	82
NSABP	89	98	16	21	4	98	115
LOCAL & OTHERS	24	25	12	14	15	25	24
TOTALS	**172**	**186**	**44**	**63**	**28**	**186**	**221**

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MEDICAL PHYSICS

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M. Stewart, R.T.(R) A.C.(T), K. Suderman, R.T.(T),
M. Tokar, R.T.(T), O. Werner, B.Sc., R.T.(NM),
C. Zeller, R.T.(T).

MEDICAL DEVICES

D. Bradley, T. Gaboury, R. Gallant, J. Legal, E. Maisey,
A. Wolk

NUCLEAR ELECTRONICS

D. Bergthorson, V. Goertzen, M. Goldie, M. Hanuschuk,
R. Shabaga, W. Stepaniuk, Y-L Sun

RADIATION PROTECTION

R. Kowaluk, R.T.(R), C. Neduzak, R.T.(R),
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D. Wylie, B.Sc.

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E. Papiez, B.Sc., G. Sandison, M.Sc., P. Therrien, B.Sc.,
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SUMMER STUDENTS

C. Cormier, J. McLellan

SECRETARIES

L. Beauchamp, T. Davidson, L. Juba, P. Kohinsky, C. Ranick

As detailed in the following pages, the Department of Medical Physics was active in a wide variety of areas. In radiotherapy, support of the clinical program involved ongoing quality control of the treatment units, dosimetry, treatment planning, operation of simulators, preparation of brachytherapy sources, provision of electronic and mechanical services, production of moulds, compensator plates, shielding blocks and much more. Rebuilding a simulator for the clinic at St. Boniface Hospital, designing and constructing shielded beds and preparing a long-range plan for replacement of therapy machines were some of the non-routine tasks carried out this year.

The support provided to nuclear medicine departments throughout the city continued to expand, both in physics activities and in mechanical and electronic technical services. The increasing sophistication of gamma cameras and their associated computers, as well as their growing number, creates a major challenge in all aspects of our work, including the preparation of tenders, installation tests, quality control, preventive maintenance and emergency repair.

Radiation protection continued to be a major activity, both in the medical centres and in other fields throughout Manitoba. More restrictive standards, combined with increased awareness of radiation safety, has led to the review of manuals, better protective devices and improved procedures.

Our close association continued with the Department of Physics, University of Manitoba. Graduate courses were given again this year, students participated in a wide variety of research projects, and gave seminars and presentations locally and at scientific meetings. The teaching load within the department continued to increase, with participation in the technologists' course, residents' program and graduate studies. Research projects were funded at the local, Provincial and National levels.

RADIOTHERAPY PHYSICS

G. Froese

The Radiotherapy Physics Section provides service in the areas of procurement and acceptance testing of equipment, quality control and use of therapy machines and simulators, brachytherapy, treatment planning and teaching.

During this year members of this section participated in a review of the need for therapy equipment, and a ten-year plan was prepared, including a recommendation for the immediate acquisition of a high energy linear accelerator. The AECB licence for the Sagittaire high energy linear accelerator expired in 1985 and an undated Safety Report was prepared as part of the application for the renewal of the licence. A used simulator has been acquired for the St. Boniface Clinic, and its total overhaul has proceeded smoothly, including a considerable number of electronic and mechanical modifications. By 1986 this new facility should be fully operational, bringing the number of simulators in Winnipeg to 3.

The quality control program for the therapy machines was improved with the introduction of a Protea Beam Analyzer. This instrument consists of a self-contained phantom incorporating ionization chambers and a readout. The MCTRF has also continued to participate in a program of the Radiological Physics Centre of the AAPM which is monitoring the output of therapy machines of a number of treatment centres using lithium fluoride dosimeters. The service of checking surface doses received by patients to sensitive areas was

also continued. A study was made of the dosimetry of irregular electron fields. Such fields are obtained by partial blocking of the field. The blocking procedure has now been standardized and a computational method has been devised to determine the output for such fields. The dose received by individual patients from such fields has been verified by film and thermoluminescent dosimetry. Additional machine accessories such as a new 30° wedge for the Theratron F cobalt unit and an improved shadow tray for the Theratron 780 cobalt unit have been designed and manufactured. Beam profiles and depth doses for the new wedge have been measured, previously existing machine data for the Theratron F have also been checked by new measurements, and the corrected data have been entered into the computer.

The AECB licence for brachytherapy sources has been renewed. Old radium needles and a defective beta ray ophthalmic applicator were disposed of and a new ophthalmic applicator has been obtained. The new applicator was calibrated and depth dose was measured with lithium fluoride dosimetry. Brachytherapy at the HSC has been moved from the ward D2 to B6. Two rooms were designed and a bed incorporating extra lead shielding was put into each room. The move to the new location required a survey with respect to radiation protection of the adjacent areas, and the training of a new nursing staff in radiation protection and care of brachytherapy patients. For the protection of staff associated with iridium 192 implants a movable and adjustable lead shield has been constructed and put into use. The quality control program in brachytherapy includes the measurement and preparation of Ir-192 seeds. A standard Ir-192 seed, calibrated by the National Bureau of Standards (USA) has been obtained and used for an intercomparison with our standard cesium 137 source. These standard sources are used to monitor the performance of our dose calibrator. Newly arrived ribbons with Ir-192 seeds are checked for the possible presence of inactive sources and for the correct spacing of seeds by preparing radiographs. For this purpose a special film cassette which is convenient to use and provides protection for the operator has been designed and constructed.

In treatment planning a new testicular shield has been designed, constructed and used clinically. Such a device is particularly desirable for the treatment of men whose radiation fields are required to be in close proximity to the gonads. During the clinical application several design modifications were proposed and when these are complete the device will be introduced into full clinical use. Existing treatment procedures continue to be scrutinized to identify any improvements that could be implemented. In the past year breast irradiation techniques and the influence of inhomogeneities in treatment of lung tumors have been studied. Dose distributions have been measured in a phantom of a breast for current irradiation procedures, and in a phantom of an arm irradiated with electrons. It is to be expected that certain aspects of our current treatment procedures will be changed in the light of these studies.

There has been a considerable commitment by members of this section to the teaching of medical physics students, radiotherapy technologists and radiotherapy residents.

TREATMENT PLANNING

M. Stewart

The treatment planning and simulator section is responsible for providing technical support for the individualized design and implementaton of treatment plans for the treatment of cancer with radiotherapy.

The simulator is an x-ray machine used for the localization of tumor volumes and marking of treatment fields on patients. During the year, the AECL Therasim was used full-time while the Picker simulator was used half-time. The total number of simulations in 1985 was 3,041, — an increase of 6% over last year. In addition, staff from this section provided assistance in doing "marker" films at St. Boniface General Hospital for the Radiotherapy patients. Marker films are taken on patients who are not sent to the Manitoba Cancer Foundation simulator but who require x-ray film to confirm the treatment area. The number of patients requiring "marker" films was 207.

The number of patients requiring the services of treatment planning was 1,038, which is an increase of 12% over last year. The procedures in this area include: designs for cerrobend shielding both with standard shields and individualized shields for field shaping totalled 905, comparable to last year; the design of lead compensators to achieve uniform dose distribution increased by 22% over last year to a total of 143; the design of treatment field arrangements and specific dose calculations totalled 275 — an increase of 32%. Use of the computer increased by 50% due to calculations which previously were done manually. Frequency of TLD measurements remained at approximately the same level as last year. Port films are taken on the treatment machine to verify the accuracy of patient positioning: 523 were taken in 1985 — an increase of 92% over 1984.

This Section continues to have a substantial commitment to the education of radiotherapy technologists both in didactic lectures and in practical training.

NUCLEAR ELECTRONICS

W. Stepaniuk

As in previous years the Nuclear Electronics Section continues to provide essential equipment service and preventative maintenance to the Department of Radiotherapy at the Manitoba Cancer Foundation and St. Boniface General Hospital, as well as the Nuclear Medicine Departments at the Health Sciences Centre, St. Boniface, Grace, Victoria, Misericordia Hospitals and also to the Nuclear Medicine Teaching Department at the Red River Community College.

A new task for the Nuclear Electronics Section this year has been to provide equipment service to the Seven Oaks Hospital Nuclear Medicine Department. The section has also undertaken the rebuilding an old Picker Therax Simulator for the Department of Radiotherapy at St. Boniface Hospital. Completion date of this project is to be March 31, 1986.

Performance of Radiotherapy and Nuclear Medicine Equipment in 1985

1. The new AECL Theratron 780 Co^{60} installed in 1984 at St. Boniface General Hospital performed with no major interruptions.
2. The Theratron F Co^{60} and the Siemens 250 KV X-Ray units continued to give dependable service with only minor interruptions.
3. The 4 MV Linear Accelerator was down for two weeks in September. This was due to a bad RF circulator followed by 2 more, defective replacement circulators.
4. The Sagittaire Linear Accelerator which at times operates 16 hours per day, continued to provide good service. The only major interruption was when the power thyratron tube and its filament transformer had to be replaced.

5. The AECL Therasim 750 and the upgraded Picker Therax simulators experienced no major problems.
6. Nuclear Medicine equipment at Health Sciences Centre had no major breakdowns and only minor interruptions during the year. The same can be said for St. Boniface Nuclear Medicine, Grace, Misericordia, Victoria and Red River Community College.

Only two major purchases were made in 1985. A new Technicare Gemini 700 Gamma Camera was purchased for the Nuclear Medicine Section at the Health Sciences Centre. The old Searle camera that it replaces will be moved to Red River Community College early in 1986, to be used as a teaching instrument for the Nuclear Medicine technologists. A GE Gamma Camera was installed in the recently inaugurated Nuclear Medicine Department at the Seven Oaks Hospital.

MEDICAL DEVICES

J. Legal

Brachytherapy utilizing iridium wire has been increasing, resulting in a demand for improved techniques. One of the requests was for a mobile shield to protect the therapist from radiation during surgical application of iridium to patients who may be lying or sitting. The heavy shield weighing approximately 100 kg is motorized so that it can be raised or lowered with a toe switch. This device incorporates adjustable wing shields to allow optimum width, it also features a lead glass window and a built in receptacle for the iridium pot. Using this shield the therapist is well protected from radiation except for hands and arms. A second simpler mobile shield reduces radiation to staff and other patients in adjacent rooms. A source calibration device and other specialized instruments has helped to streamline this growing method of treatment.

Reference was made in the 1984 report to a pair of "lead beds" which were designed to shield staff and patients in adjacent rooms and the floor below from patients being treated with radioactive sources. These heavy lead shielded beds weighing over 600 kg were primarily designed for cesium patients, but it appears they are useful for iridium patients as well. Both beds are now installed on B6 and seem to perform as expected and have been well accepted by patients and staff.

Three technetium generators built over the past 10 years for Radiopharmacy have now been overhauled and upgraded. We expect them to continue to function for many years to come.

Federal regulations regarding intracity transportation of radioactive liquid isotopes have become more stringent lately, requiring the development of a new system of packaging. Small glass vials are now shipped in a sealed steel container with custom foam inserts which protects against breakage in virtually any conceivable impact.

An assortment of acrylic devices were designed to shield personnel when handling P 32.

A specialized gas mixing apparatus was built for an anesthesia research project.

An ongoing research project using the CT scanner required a phantom with a calcium carbonate ring to simulate the skull.

A large flood phantom was built to calibrate the new SPECT gamma camera now in service on G3.

Another phantom was built to simulate a lung with circulating blood to be used during hyperthermia research experiments.

An elaborate custom designed mobile cabinet was built to accommodate the computerized S + 4 Coulter counter and all the peripherals.

A number of cardiac injector stands and related accessories were built for the ICU ward.

The mould room patient load increased dramatically over the past year. 540 patients were referred with many returning for subsequent fittings accounting for 1,049 visits. This represents a 30% increase over 1984.

Total sealed source deliveries seemed to have decreased somewhat from 286 trips the previous year to 212 in 1985. The breakdown is as follows. Cesium — 156, Beta plaque — 28, Gold grain — 0, Iridium ^{192} — 28.

We continue to train Premed and Radiotherapy technology students — 10 in 1985. We also responded to requests for specialized vacuum formed products such as organ isolation vessels, simulation models for peritoneal dialysis, pressure masks for burn victims, battery covers for wheelchairs and iridium applicators for ears and other anatomical features.

RADIATION PROTECTION

A. M. Sourkes

In 1985 the Radiation Protection Section (RPS) continued administration of X-Ray Safety Regulation 207/79 under the Public Health Act and increased enforcement activities of Manitoba Regulation 207/77 with respect to radiation hazards under Chapter W210 of the Workplace Safety and Health Act for the Departments of Health and Environment, Workplace Safety and Health.

Under the X-Ray Safety Regulation, the major effort of the RPS was in surveying of the x-ray units throughout the Province. The RPS continued to act as the intermediary for the TLD (thermoluminescent dosimeter) plaque radiation monitoring service in use by the 4500 x-ray workers in the Province. This responsibility includes checking for proper usage of the service by the 550 groups involved, registering and deregistering groups as required, investigating undue exposures and compiling an annual summary of all exposures.

Under the Workplace Safety and Health Act, in the area of non-ionizing radiation protection a total of 511 inspections were carried out. Approximately 65% of these inspections were at industrial-commercial locations and 35% were at medical and paramedical facilities. Examples of potentially hazardous non-ionizing radiation emitting devices surveyed during the inspections are induction heaters, radio-frequency glue dryers, leather dryers, heaters, sealers and diathermy devices; ultraviolet light platemakers, blue line, silk screening, and camera lamps, ink curing and suntanning lamps, ultrasound therapy devices, construction, industrial, research, ophthalmological and display lasers. In addition to the inspections and survey work, 23 information packages were sent to concerned groups and individuals in response to enquiries about radiation emissions from video display terminals.

Other activities included the provision of consulting services to the Department of Environment and Workplace Safety and Health, response to public inquiries on ionizing and non-ionizing radiation matters, the delivery of radiation safety lectures on request, emergency response to incidents involving the use or transport of radioisotopes, the performance of wipe test analyses for isotope licencees and the design, inspection and approval of new

x-ray facility barrier installations. The environmental radiation monitoring program of ground and surface waters in the vicinity of the Underground Research Laboratory (URL) in southeastern Manitoba continued with the monitoring accommodating sampling requests by area residents; and with participation on the newly formed URL Steering Committee. The advisory committee on radioactivity has been expanded to include consideration of the presence of radon in dwellings. As well, participation in the national technical committee dealing with the management of low level radioactive waste continued in 1985.

SUMMARY OF 1985 X-RAY MACHINE REGISTRATION AND INSPECTION DATA

Type of Installation	Total Registered	In Service	Surveyed in 1985	Approved Initially	Corrected & App. During Survey	Approval Withheld	Approved Subsequently
Chiropractic	38	34	24	19	0	5	3
Dental	785	769	209	179	9	21	19
Educational	58	47	34	32	0	2	2
Hospital	169	162	135	114	0	21	21
Industrial	29	27	6	5	1	0	0
Lab & X-ray	124	124	112	84	1	27	23
Medical Off.	74	72	67	51	1	15	15
Veterinarian	74	74	28	15	2	11	6
Totals	**1,351**	**1,309**	**615**	**499**	**14**	**102**	**88**

SUMMARY OF 1985 NON-IONIZING RADIATION INSPECTIONS

Type of Inspection	Surveyed in 1985	Approved Initially	Corrected and Approved During Survey	Approval Withheld	Approval Subsequently
Industrial and Commercial Facilities					
Lasers	28	11	14	3	3
Radio-frequency Devices	24	5	12	7	1
Microwave Devices	15	15	0	0	0
Ultraviolet Radiation Devices	181	98	60	23	17
Miscellaneous Devices	80	80	0	0	0
Medical Facilities					
Lasers	5	3	2	0	0
Radio-frequency Devices	25	6	19	0	0
Microwave Devices	7	7	0	0	0
Ultraviolet Therapy Devices	122	58	44	20	12
Ultraviolet Radiation Devices	24	4	18	2	2
Totals	**511**	**287**	**169**	**55**	**35**

RADIATION PROTECTION ACTIVITIES

Activity	Number
Protective Barrier Room Design Approvals	110
Protective Barrier Installation Inspections	62
Dosimetry Exposure Investigations	58
Wipe Sample Analysis	194
Response to Public Inquiries	434
Radiation Safety Lectures	21
Mail-In Dental Unit Checks	489
Non-Ionizing Device Surveys	511
X-Ray Machine Inspection	615
Miscellaneous Surveys	21

NUCLEAR IMAGING

R. Palser

During 1985 the Nuclear Imaging Section has continued its traditional role of providing clinical service to Manitoba nuclear medicine departments in the areas of equipment purchase and optimum use, developmental research, radiation protection and teaching. In addition, a number of projects have been undertaken with the radiology departments at the Health Sciences Centre and St. Boniface General Hospital.

At the Health Sciences Centre the Elscint single photon emission computed tomography gamma camera (SPECT) system, installed late in 1983 was the subject of an extensive evaluation. As a result of this the detector gantry was replaced by the company and several smaller modifications made to achieve better clinical performance. The computer software has been upgraded to make the system somewhat easier to operate, and a number of clinical programs and procedures developed on the machine.

Also, at the Health Sciences Centre a Technicare large field of view gamma camera has been ordered and will be delivered in the first few months of 1986. This machine is unusual in that it has a large square detector, rather than the conventional round one, and will considerably reduce the imaging time required for bone and whole body diagnostic procedures.

At St. Boniface General Hospital a single photon emission computed tomography system is being evaluated for purchase in 1986. The new clinical modality of bone densitometry useful in the diagnosis and management of patients with metabolic bone disease, has been under intensive review and equipment selected for delivery in 1986. At the Seven Oaks General Hospital a General Electric large field of view gamma camera was purchased, installed and acceptance tested during the year. It is now in routine clinical use.

In conjunction with the Radiology Departments at St. Boniface General Hospital and the Health Sciences Centre, the section has become heavily involved in evaluation of the new imaging modality of Magnetic Resonance Imaging (MRI). To prepare for the eventual acquisition of an MRI machine, we have assisted the hospitals in interpretation of the technical specification and operation of these machines, participated in the organization of an MRI symposium, attended summer school training courses, made site visits to the University of British Columbia and the Montreal Neurological Institute facilities, and are undertaking a joint MRI research program with the Universities of Winnipeg and Manitoba.

A number of smaller projects related to equipment evaluation, purchase and acceptance testing for various city hospitals were completed during the year. Dose calibrator, thyroid uptake probe, radiation shielding and radioactive calibration source evaluations were made. An evaluation was made of the design of x-ray filters for use by the Children's Hospital in the diagnosis of patients suffering from scoliosis. Acceptance tests were performed on an image intensifier system installed at St. Boniface General Hospital.

The Nuclear Medicine quality control program covers all clinically used gamma cameras, uptake probes, radiation monitoring equipment, well counters and some of the film processors in the city hospitals. The program regularly reviews the performance of each item with the intent of maintaining long term optimal and stable operational characteristics and predicting the useful lifetime of each piece of equipment.

In the area of radiation protection and safety, the section was active in providing services to the city hospitals, the Manitoba Cancer Treatment and Research Foundation via the Clinical Isotope Committee, the Therapy Sources Committee, and the Workplace Safety and Health Committee.

During the year members from the section have been involved in teaching courses in the Graduate Physics Program of the University of Manitoba, offering two courses to Nuclear Medicine residents, participating in radiation protection courses offered at the University of Manitoba, as well as presenting several lectures related to topics in medical physics.

ACADEMIC ACTIVITIES

The Medical Physics seminars were held on a weekly basis with 20 presentations being given on various topics. Participants included staff from the Cancer Foundation, University of Manitoba, as well as guest speakers from other centres in Canada and the U.S. The talks given covered a wide variety of subjects pertaining to medical physics, biophysics and radiation physics.

The Medical Physics Graduate Program is organized under the auspices of the Physics Department in the Faculty of Science at the University of Manitoba. There are currently a total of 2 Ph.D. students and 5 M.Sc. students.

Staff members involved in the Medical Physics Graduate Program have faculty appointments in departments of the University of Manitoba and offer the following courses subject to student enrollment.

Course Number	Title	Presenter(s)
16.736	Medical Radiation Physics	Dr. R. F. Palser
16.737	Radiotherapy Physics	Dr. P. Dunscombe
16.738	Radiation Biology	Dr. G. Froese
16.739	Radiation Protection	Dr. W. Huda/Dr. A. M. Sourkes
16.740	Medical Imaging	Dr. S. Shalev/Dr. T. Lee
16.741	Diagnostic Methods	Dr. S. Shalev/Dr. T. Lee

The courses are open to all eligible students at the U of M and have been taken by the M.Sc. and Ph.D. Medical Physics students, graduate students in the Physics department at the U of M and also by occasional students at the U of M.

Details of the students in the Medical Physics Graduate Programme are shown below in summary form.

Student	Degree	Research Topic	Academic Supervisor
G. A. Sandison	Ph.D.	Electron Dosimetry	Dr. W. Huda
J. Bews	Ph.D.	Imaging	Dr. Shalev
P. Therrien	M.Sc. (Research)	Radiotherapy Optimization	Dr. S. Shalev
T. Constable	M.Sc. (Research)	Hyperthermia	Dr. P. Dunscombe
A. Tsoukatos	M.Sc. (Research)	Hyperthermia	Dr. P. Dunscombe
E. Papiez	M.Sc. (Research)	Electron Dosimetry	Dr. G. Froese
D. Lowe	M.Sc. (Research)	Dosimetry	Dr. R. Palser

MONOCLONAL ANTIBODIES TO MOUSE TUMOR CELLS

G. Froese

Further studies have been carried out to characterize our syngeneic antibody to the 1509a mouse sarcoma. The antibody is produced by a previously isolated hybridoma. More extensive purification of the IgM-antibody has made it possible to investigate the inhibitions of the binding of ^{125}I-labelled antibody by unlabelled antibody and thus to obtain more quantitative data on the specific binding. Variations in the expression of the life cycle of the cells and under different growth conditions may give more information about the functional role played by the antigen.

LEAD IN BONE ANALYSIS BY XRF

R. F. Palser and W. Huda

The project developed an X-ray fluorescence spectroscopy (XRF) technique to perform the in vivo detection and quantification of lead (Pb) uptake in bone. The method has an estimated detection limit of about 25 parts per million and is therefore only expected to be useful in analyzing the elevated Pb in bone levels that are expected to be found in individuals who are occupationally exposed to Pb. Over 300 individuals have had measurements performed to assess the Pb content of their right and left index fingers. About 30% of the 200 occupationally exposed individuals were found to have significant Pb in bone burdens. For these individuals, a weak correlation was found between the Pb in bone measurements and the individual's age and a strong correlation between the Pb in bone burden and the length of time spent in the Pb industry. There was no significant correlation between Pb in bone and Pb in blood measurements which supports the theory that the former measures long term cumulative exposure and the latter assesses recent, acute exposure to this toxic agent.

CT DOSIMETRY

W. Huda and G. A. Sandison

The project was aimed at developing a radiation risk approach to CT dosimetry. All experimental work and the data analysis have now been completed. The genetic and somatic detriment associated with the 9 year operation of the EMI 5005 CT scanner at the HSC has been completed. For the 50,000 individuals scanned, the genetic detriment to all future generations is negligible. The somatic detriment has been established to be the induction of

about one cancer which is considerably smaller than the detriment associated with the iodine contrast agents used in 76% of the CT examinations. The work has been extended to assess the detrimental risks to staff and patients associated with conventional X-ray procedures and with Nuclear Medicine scans.

ELECTRON DOSIMETRY

G. A. Sandison and W. Huda

The project is aimed at developing a pencil beam approach to electron dosimetry for accurate electron beam treatment planning.

A theoretical formalism based on the Fermi-Eyges multiple small angle scattering theory has been applied to the electron beams from the MCF Sagittaire linear accelerator. Experimental verification of theoretical work is performed, using the Sagittaire and standard dosimetric techniques. The theory developed predicts penumbra in open or shielded beams for the beam energies, Source Surface Distances (SSD), and electron field sizes normally used clinically. The theory is accurate in the air space above patients but breaks down at depth in tissue due to the neglect of delta ray production, large angle scattering and bremstrahlung production.

Current work includes the intercomparison of three independent methods of parameterizing the Sagittaire electron beams and the modification of the Fermi-Eyges pencil beam formalism to take into account the physical interactions that the theory currently neglects. Collaborative ventures in the field of electron dosimetry are being planned with groups working in this field in Minneapolis, Minnesota and Edmonton, Alberta.

PATIENT ACTIVATION DURING HIGH ENERGY PHOTON RADIOTHERAPY

P. B. Dunscombe and W. Huda

It is known that short lived positron emitting isotopes, principally ^{11}C, ^{13}N, and $^{15}0$, are produced within the treatment fields of patients irradiated with high energy photons. Counting equipment has been set up and some preliminary data taken to establish the magnitude of this effect. It is proposed to examine the feasibility of imaging the induced activity following treatment with a view to identifying and quantifying any clinically significant metabolic or blood flow information which may be present.

MEASUREMENT OF REGIONAL CEREBRAL BLOOD FLOW AND XENON PARTITION COEFFICIENT IN PATIENTS WITH GLIOBLASTOMA MULTIFORME

T. Lee, D. I. Hodson, P. B. Dunscombe, M. Kroeker, B. McClarty*, M. West+, R. Ellis*

*Radiology, St. Boniface General Hospital
+Surgery, St. Boniface General Hospital

Regional cerebral blood flow (rCBF) and xenon partition coefficient (rXePC) in glioblastoma patients undergoing radiation treatment are to be measured by xenon enhanced computed tomography (CT). The aims of the project are twofold: (1) to investigate the potential of regional blood flow in the tumour as a prognostic indicator of patient survival; (2) to investigate whether radionecrosis of normal brain tissue, manifested as changes in rCBF and rXePC, occurs as a result of radiation treatment of the patient.

In preparation for the clinical studies, a series of experiments with a brain phantom has been performed. From the results of these experiments, the optimum technique (kVp) for xenon enhanced CT scanning has been determined and procedures for deducing xenon concentrations from CT numbers have been found. The next stage is the construction of the breathing apparatus for the administration of xenon gas to the patient. Patient studies are planned for the summer of 1986.

APPLICATION OF LINEAR MODELLING TO DYNAMIC RADIONUCLIDE STUDIES

*T. Lee, D. Greenberg**

*Nuclear Medicine, Health Sciences Centre

The project involved the data analysis of dynamic radionuclide studies performed in the Nuclear Medicine Department, Health Sciences Centre. A method to quantify the renal extraction efficiency of the scanning agent, Tc-99m DTPA, from a dynamic kidney study without blood sampling at the renal artery and vein has been developed. When the method is applied to a group of patients with different types of renal disease, the values determined for the extraction efficiency of Tc-99m DTPA in the patients are above the expected normal value. Incorporation of this method in routine clinical studies is currently in progress.

In the past year the computer-gamma camera system used in the data acquisition of patient studies has been replaced by a more modern and large field of view type. This has resulted in the rewriting of most of the data analysis software. The liver studies, which are also amenable to linear modelling, will continue when the necessary modification to the software is completed.

WHOLE BODY DOSIMETRY

R. Palser, M. Billinghurst, J. B. Sutherland**

*Department of Radiology, Health Sciences Centre

The object of this study is to measure the radiation dose distribution to various body organs resulting from the injection of Technetium labelled bone seeking radiopharmaceuticals. Two gamma cameras were obtained, mechanically modified and electronically interfaced to a data acquisition computer. The system has been calibrated and collection of patient data begun.

CLINICAL HYPERTHERMIA

P. B. Dunscombe, K. Malaker

1985 saw the clinical introduction of a full hyperthermia facility including a localized microwave applicator, forced air surface cooling and a microcomputer controlled thermometry system. The equipment functioned reliably and was shown to be able to safely produce a temperature rise in the therapeutic range above 42°C. Subjective responses of the patients referred for this modality were favourable although it is too early to attempt to quantify the clinical benefit of this new form of therapy.

Investigational efforts continued to be directed towards the area of thermal dosimetry. Self heating of the thermocouple thermometers used in the clinic has been quantified and the consequences of this effect on clinical dosimetry are being studied theoretically.

Blood flow through and around the heated tumour is of major significance in determining the temperatures achieved during hyperthermia. A thermal washout technique to detect and measure any changes due to temperature elevation is being examined both experimentally and theoretically.

EVALUATION OF DIGITAL ENHANCEMENT OF PORT FILMS

S. Shalev, C.-W. Cheng, K. Malaker

Precision radiation therapy requires the verification of beam locations by exposing port films during treatment. Such films have low contrast and poor spatial resolution, and can be improved by various enhancement techniques. We have examined the relative merits of digital and photographic enhancement by means of a set of films exposed to a test object consisting of thirteen cylinders of varying thickness, each with a small notch. A wide selection of observers viewed the films, and their scores in correctly identifying the cylinders and notches were analyzed in terms of the type of film and enhancement technique, type of observer and other factors.

QUANTIFICATION OF RADIOTHERAPY TREATMENT PLANS

S. Shalev, P. Hahn, P. Therrien, L. Bartel

The use of isodose plots to evaluate and compare alternative treatment plans is difficult, subjective and time-consuming. In cases of multiple planes, non-coplanar beams or complex arc therapy, the value of such plots is very limited. We have developed a simple technique in which "images of regret" present the differences, if any, between a plan under consideration and the prescribed dose distribution. Quantitative comparison is made by a set of score functions, indicating the degree of compliance of each scored parameter with the prescribed requirements and limits of acceptability. The method has been applied to ca prostrate, using CT scans to identify the target volume and sensitive organs such as rectum, small bowel and head of femur. Work is in progress to generalize from single planes to volumetric scores and dose histograms for each organ. Dose response curves are being used to determine risk of complications for each plan under consideration.

DEPTH PERCEPTION FOR MULTI-SLICE DATA SETS

*B. Kettner, S. Shalev, C. Lavelle**

*Faculty of Dentistry, University of Manitoba

We have developed a technique for pseudo-3D reconstruction of CT scans, using the inexpensive DICOM-8 digital imaging computer. Scan data are transferred from magnetic tape, mapped to 7 bits in depth and to an operator-defined region of interest in area. The operator has interactive control over the form of the 3D display, using selective transparency to remove overlying organs, or geometrical cuts to expose internal structure. Depth clues include shading, an external frame and oblique projections in any of 18 different viewing angles. 3D images are presented in pseudo-colour on a 512x512x8 bit image plane, and may be derived from up to 128 CT scans. Examples include head and pelvic images. Studies with this technique include the evaluation of anomalous craniofacial form, visualization of drainage tubes in a hydrocephalic patient, and volumetric radiotherapy treatment planning.

THE PHYSICS OF DIAPHANOGRAPHY

S. Shalev, J. Linford, J. Bews, H. Schipper, R. Brown**
*St. Boniface General Hospital

Work continued on the investigation of light transmission through cell suspensions and human tissue samples. Several types of cells were investigated, and empirical expressions were derived from the extinction of a narrow light beam when traversing homogeneous suspensions of various concentrations. Normal and pathological specimens of human breast tissue were studied with light in the near infra-red, and techniques developed to identify cancerous lesions by means of differential spectral analysis. A tissue-equivalent medium was developed for the construction of phantom for precise imaging studies, quality control and equipment calibration.

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ONCOLOGY SOCIAL WORK

DIRECTOR — B. S. H. Wong., M.S.W., R.S.W.

SOCIAL WORK STAFF

Beatrix Pociwauschek, B.S.W., R.S.W.

SUPPORT STAFF

Karen Yaremchuk, Anneliese Friedle

SOCIAL WORK STUDENT

Carolyn Voort

The Department of Social Work was established eleven years ago by the Health Sciences Centre and the Manitoba Cancer Treatment and Research Foundation. Since that time the Oncology Social Work Program has been developed, coordinated and staffed by professionally trained social work personnel.

I. Patient Care

Our primary focus is to provide counselling services to those who experience difficult and stressful times in their lives when they encounter cancer. Over the years, we have witnessed that some people have great difficulties accepting the initial diagnosis; others have various problems during treatment; still others experience extreme anxiety during the period of remission not knowing when recurrence might come; another group have great fear dealing with the inevitable death and subsequent bereavement for their families. Under stress family and other relationships, come into conflict. Proper assessment, recommendation and ongoing counselling require professional attention. Without early social work intervention, these cases can become unmanagable on a later date and subsequently require psychiatric consultation and treatment.

Referral services comprise a large portion of our case load. Long term illness and treatments often disrupt employment. Patients and families seldom have the means to sustain themselves during this period of illness. Consequently, they will have to be referred to the appropriate community agencies for financial assistance.

Cancer debilitates many of our patients to the point that they can not continue to live at home. This is particularly true for the elderly and those living alone. Supportive services such as V.O.N., Homemaker and Meals on Wheels are often provided through the Home Care Department, enabling them to continue to function independently in the community. At a certain stage these patients require more services than Home Care can provide. When these circumstances arise alternative placement plans have to be considered. One of the alternatives is often a referral to a palliative care setting such as the Princess Elizabeth Hospital. Intervention on our part is frequently necessary before the patient and family accept the P.E.H. placement. The actual transfers of inpatients to other institutions are handled by the social work assistant at H.S.C.

Being an outpatient facility, those who need admission are hospitalized at the H.S.C. Besides our own physicians a multidisciplinary team of the H.S.C. will also be involved in the care of our patients. This large system of operations involving so many people often confuse the patient as well as family members. Social Work can take on the coordinating function to set up case or family conferences in order to facilitate communication among all those involved in the care of these patients.

Statistics: Social Work consults from clinic, H.S.C. and community

	1982	1983	1984	1985
New Patients	201	216	234	234
New Mastectomy Patients	88	57	70	72
Total	**289**	**273**	**304**	**306**

Ideally, mastectomy patients should be seen preoperatively. However, practice has indicated that this is not possible. A few years ago informal discussions with several surgeons and surgical nurses took place resulting in an understanding that all new mastectomy patients would automatically be referred to our department for appropriate services. A majority of these cases only needed to be referred to the Mastectomy Volunteer Visitation team for practical information. A small number of this group remained with us for ongoing counseling.

II. Education:

Oncology Social Work continues as a student field placement for the School of Social Work, University of Manitoba. For the past five years the teaching responsibility for these students had been shared between the University Supervisor and the Agency Supervisor. During the year under review this has been changed to the Agency Supervisor taking on the total teaching responsibility.

During this academic year, the Faculty of Nursing, U. of M. discontinued their B.N. student field experience with us after five years of association. This change came about due to their program concentration on the pediatric population.

Oncology Social Work continues to be involved in the education of students of other disciplines, (R.T. students).

III. Other Involvements

1. *Social Work — Nursing Rounds:*

Two sets of weekly rounds have been held between social work and chemotherapy and radiotherapy nursing. These rounds have served a threefold purpose:

1) Service to patients: Regular communication between disciplines has led to early problem identification and appropriate referral.

2) Education: Through case discussions, these rounds have provided a forum of education for students of all disciplines.

3) Mutual staff support: These rounds have provided the opportunity for interdisciplinary understanding and mutual support.

2. *Co-ordinating Committee*

During the year under review new members have joined this committee of Foundation middle management personnel and department heads. As the committee continues into its second year of operation, it is quite evident that it has served the function of improving communication between the departments in regard to day to day problems and issues. A major project undertaken by the committee has been the development of an information brochure for new patients.

3. *Oncology User Group*

In the Fall of 1985 this group, comprised of medicine, nursing and representatives from all other disciplines involved in the care of cancer patients, was called together to examine the "Oncology Unit Proposal, General Hospital, H.S.C.". The establishment of an oncology inpatient unit for adult cancer patients has been long overdue. It is with great anticipation that this much needed unit, which will hopefully incorporate the palliative care component, will become a reality in the near future.

IV. Public Relations

Oncology Social Work has frequently been called upon to provide consultation to our colleagues in the community. Many non-patient related inquiries are referred to this department for exploration and appropriate responses.

BREAST CANCER SCREENING UNIT

Medical Director:	Dr. David Bowman
Co-ordinator:	Patricia Edward, B.S.N.
Surgeons:	Dr. Wayne Beecroft
	Dr. T. Kenneth Thorlakson
Radiologists:	Dr. George Hardy
	Dr. Harold Standing
Pathologist:	Dr. H. Yazdi
Nurse Examiners:	Madeline Blanchard
	Ann Crossin
	Jeanette Kosteniuk
	Valerie Powell
	Margaret Sawyer
	Elisabeth Weiler
Radiographers:	Norma Einarson
	Virginia Kowalski
	Barbara Moore
Secretaries	Maria DiBiase
	Romona Brown

The Manitoba Unit of the National Breast Cancer Screening Study, initiated in 1981, continues to screen healthy female volunteers for breast cancer.

The Study is designed to:

- determine the extent to which mammography (MA) is responsible for reducing death rates in well women volunteers aged 50 to 59 years.
- determine whether death from breast cancer is reduced in well women volunteers aged 40 to 49 who are screened by mammography and physical examination annually for five years compared to volunteers allocated to a control group.
- analyze the contribution of various risk factors in prognosticating the development of subsequent breast cancer.
- analyze the cost effectiveness of breast screening.
- provide detailed information regarding the natural history of breast cancer as detected in such a regular screening programme.

Beginning in June, 1985, the final rescreening visits began, the fifth annual examinations for participants committed to five visits as directed by the Study Protocol. All volunteers 40-49 years of age randomized to Mammography, as well as the 50-59 year old women randomized to the Control Group were being seen and examined and issued with their earned citation: LEASE ON LIFE. By year's end, all registrants entering the Programme in June, July, and August had completed their commitment. The total number of visits to the Unit equalled 6,184; total number referred to REVIEW CLINIC (for surgeon's exam) = 241; total Tissue Biopsies recommended = 51.

Recall returns have averaged 92% (of requested appointments).

TABLE I
Volunteer Recruits in Screening Study

	(1984)	1985	Cumulative Accrual (1981-1985)
Total volunteers registered	677	—	10,114
Total randomized to "Control"	338	—	5,054
Total randomized to MA	339	—	5,060
Total Cancers detected	24	21	106
By age group:			
40-44	3	3	14
45-49	5	5	27
50-54	8	8	36
55-59	8	5	29

Women between the ages of 40-49 years, not allocated to Mammographic examination continued to respond to their annual questionnaires which detailed their practice of Breast Self-examination and interval interventions if one had been required.

Speaking requests are also honored by the Study Co-ordinator on local television and among groups of women conducting educational presentations for their membership. A class to the Student Nurses at Red River Community College was conducted; two reports on Breast Self Examination were requested both by the Licensed Practical Nurses' and the Women's Institute of Manitoba.

The Nursing Staff within the Unit were pleased to be a part of the educational preparation of four registered nurses, themselves participants in the Program, who, under the direction of Dr. Audrey Johnson, La Verendrye General Hospital, Fort Frances, Ontario, opened a Breast Education Programme in their hospital for the purpose of physical examination of volunteer women wishing a Breast Examination and instruction in Breast Self Examination. Their Unit opened on November 14, 1985.

We continue a close referral network with the Diaphanography Programme, and provide educational experiences for the students in the MCF Radiotherapy Technicians Programme.

It is anticipated the Manitoba Unit of the National Breast Screening Study will have completed its mandate by early spring, 1987.

MANITOBA INSTITUTE OF CELL BIOLOGY

Director — G. J. Goldenberg, M.D., Ph.D., F.R.C.P.(C)

A. Begleiter, Ph.D.
L. J. Brandes, B.Sc., M.D., F.R.C.P.(C)
D. Chow, Ph.D.
J. G. Dodd, Ph.D.
J. M. Gerrard, M.D., Ph.D.
A. H. Greenberg, M.D., Ph.D.
E. D. Israels, B.A., M.Sc., M.D.
J. Johnston, M.D., F.R.C.P.(C)
N. Kobrinsky, M.Sc.(Med.), M.D., F.R.C.P.(C)
H-Y. P. Lam, Ph.D.
S-T. Lee, Ph.D.
M. Mowat, Ph.D.
F. Paraskevas, M.D.
B. A. Schacter, B.Sc.(Med.), M.D., F.R.C.P.(C)
J. A. Wright, B.Sc., M.Sc., Ph.D.

GRADUATE STUDENTS

C. Anhalt, E. Atkinson, R. Bennet, R. Blosmanis, A. Chan, D. Creasey, J. Damen, S. Egan, J. Hickerson, J. Hicks, R. Kraut, L. Miller, V. Miller, T. Osachuk, E. Roussell, P. Sandstrom, C. Seneviratne, A. Tagger, D. Tough, S. Uniyal.

FELLOWS

A. Deffie, S. Dogra, M-C. Gingras, S. Israels, N. Khalil, G. McClarty.

B.Sc.(MED) SUMMER STUDENTS

J. Boux, T. Davie, L. Ebbeling, K. Harrop, R. Hastman, E. Hildes, P. Kerr, G. Lacey, B. Lavallee, T. Lesiuk, A. Merry, J. Ormiston, J. Teoh.

TECHNICIANS

L. Beattie, G. Blair, P. Bogdanovic, A. Chan, M. Cawker, M. Chapiel, V. Cripps, K. Devine, J. Dickson, E. Friesen, G. Gowen, L. Heinemann, J. Hellsten, L. Jarolim, M. Jesson, D. Johnson, I. Kostolansky, M. Leith, S. Leveque, A. Low, J. Maeba, J. Morgan, B. Ottenbreit, S. Ozomoto, L. Pugh, P. Robinson, M. Sauder, R. Singal, S. Singhroy, M. Talgoy, C. Ulicki, M. Wilcock, P. Wingert.

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ANIMAL ATTENDANT

E. Ahola

SECRETARIES

L. Devlin, D. Faulkner, S. Geisler, S. Ireland, M. Kosheluk.

THE MANITOBA INSTITUTE OF CELL BIOLOGY

The Manitoba Institute of Cell Biology was founded jointly by the University of Manitoba and the Manitoba Cancer Treatment and Research Foundation in 1969. The purpose of the Institute is to carry out interdisciplinary research and training in the basic and clinical aspects of cancer and other diseases by studying disease mechanisms at a cellular level. The Institute of Cell Biology is governed by an independent Board of Management consisting of eleven members, three appointed by the University of Manitoba, three appointed by the Manitoba Cancer Treatment and Research Foundation and five jointly appointed by both sponsoring Institutions. The Manitoba Institute of Cell Biology is housed in the Manitoba Cancer Treatment and Research Foundation adjacent to the Faculty of Medicine, University of Manitoba and the Health Sciences Centre.

The Institute of Cell Biology consists of a Director, sixteen senior investigators, and eighty-one staff including Postdoctoral Fellows, graduate students, summer students, technicians, laboratory assistants and animal attendants. Although the Institute of Cell Biology is not a degree-granting body, advanced degrees at the Masters or Ph.D. levels may be obtained by special arrangement with any of the departments in the Faculty of Medicine, University of Manitoba. The major emphasis of the research program of the Institute of Cell Biology has centered on the fields of Oncology, Hematology, Molecular Biology and Immunology. Senior investigators in addition to holding appointments in the Manitoba Institute of Cell Biology also hold cross-appointments in a wide range of University departments including the Departments of Immunology, Genetics, Biochemistry, Physiology, Medicine, Surgery, Pediatrics, Obstetrics and Gynecology, and Microbiology. Other members also have acted as Adjunct Professors in these and other basic science departments, particularly while supervising the thesis work of a graduate student pursuing an advanced degree at either the Masters or Ph.D. level.

The location of the Manitoba Institute of Cell Biology in the Manitoba Cancer Treatment and Research Foundation building has enabled the development of a parallel program of basic and clinical investigation of patients with neoplastic disease. Of particular interest has been the development of tumor immunology, molecular biology and experimental chemotherapy in which patients with a wide range of neoplastic disorders are available for investigation conducted by senior investigators in the Institute of Cell Biology. Not only is this interaction facilitated by a geographical juxtaposition of the two Institutions, but also by the fact that many senior investigators hold cross-appointments in the Manitoba Institute of Cell Biology and the Manitoba Cancer Treatment and Research Foundation.

A wide range of research programs was in operation during 1985. Featured prominently in the research activities of the Institute were tumor immunology, molecular biology and biochemical pharmacology. Studies on natural resistance mechanisms in the immune response of the host to tumors support the role of natural killer cells and natural antibody in antitumor surveillance. A novel macrophage activating cytokine was identified in the large granular lymphocyte. Other studies on anti-suppressor activity indicate that anti-suppression may play a pivotal role in immune stimulation and unresponsiveness. Major advances in elucidating the T cell pathway in antisuppression have been made. A wide-ranging program in somatic cell genetics has focused on the central role that the enzyme ribonucleotide reductase may play both in differentiation, cell proliferation, senescence and cell proliferation. Resistance to the drug hydroxyurea, a chemotherapeutic agent, was

found to be associated with increased production of the enzyme. The development of molecular biology programs within the Institute of Cell Biology has progressed significantly in the last year. Altered expression of the p53 cellular oncogene in erythroleukemia was recently identified and molecular cloning of the p53 gene from lines exhibiting rearrangements has identified a major deletion. Studies have also been initiated this last year on the role of the H-*ras* oncogene in metastasis formation and tumor progression. A strong association between metastatic efficiency and oncogene expression was identified, and evidence of gene amplification and rearrangement found in metastatic lung tumors. Promising new results on the expression of the *myc* oncogene in human benign prostatic hypertrophy and carcinoma of the prostrate have been published. Measurement of mRNA levels and *in situ* cDNA-mRNA hybridization identified high levels of *myc* expression in these prostatic diseases. Recent work on the role of the inositol cycle in platelet activation support the concept that inositol triphosphate is a major intracellular messenger in platelets and that his pathway may promote phosphorylation of proteins which are associated with platelet granule mobilization. Studies in experimental chemotherapy and biochemical pharmacology of cancer chemotherapeutic agents explored the role of quinone antitumor agents and diethylstilbesterol on the induction of DNA single and double strand breaks. Evaluation of the biochemical changes in chronic lymphocytic leukemia and Hairy cell leukemia following treatment with 2;-deoxycoformycin is continuing. A new compound which is selective for the antiestrogen binding site (DPPE) has been identified and appears to have important histamine receptor antagonist properties. This compound may have a number of novel physiological effects based upon its interaction with a histamine-like receptor.

To provide additional background information on the nature and type of research programs being conducted in the Manitoba Institute of Cell Biology a series of research abstracts and publications is presented for each of the senior investigators.

THE INTERACTION OF 3'-(3-CYANO-4-MORPHOLINYL)-3'-DEAMINOADRIAMYCIN (CMA) AND RELATED ADRIAMYCIN (ADR) ANALOGS WITH DNA IN HT-29 HUMAN COLON CARCINOMA CELLS IN VITRO

Asher Begleiter, Michael I. Jesson and James B. Johnston

The Adriamycin analog, CMA, is the most potent anthracycline prepared to date. It is 100-to 1000-fold more potent than ADR in HT-29 human colon carcinoma cells and other tumor cells. We have compared the interaction of CMA, ADR, and the related ADR analogs 5-imino-3'-(3-cyano4-morpholinyl)-3'-deaminoadriamycin (ICMA), 3'-(4-morpholinyl)-3'-deaminoadriamycin (MA) and 5-imino-3'-(4-morpholinyl)-3'-deaminoadriamycin (IMA) with DNA in HT-29 cells using elution assays. The cyanide containing analogs CMA and ICMA produced significant DNA-DNA crosslinking. Incubation of cells for 2 hr with 40 nM of CMA produced approximately 150 rad equivalents of crosslinks. A similar incubation with an equitoxic concentration of ICMA (20 μM) resulted in approximately 250 rad equivalents of crosslinks. Equitoxic concentrations of ADR, MA or IMA produced no significent crosslinking. Elution assays without proteinase K showed no increase in crosslinking with either CMA or ICMA, indicating that neither of these agents produced DNA-protein crosslinks. These studies provide evidence that DNA-DNA crosslinking is an additional mechanism of action that may account for the

potent antitumor activity of CMA. Since only CMA and ICMA produced DNA-DNA crosslinks, the crosslinking activity of these anthracyclines may require the presence of a cyanide group. The observed difference in crosslinking activity between CMA and ICMA suggests that the quinone group may be involved in the crosslinking mechanism.

ANTITUMOR ACTIVITY OF QUINONE ANTITUMOR AGENTS IN QUINONE RESISTANT TUMOR CELLS

Asher Begleiter and Marsha K. Keith

Previous studies have shown that a quinone group in the structure of a compound can result in antitumor activity and in the production of DNA strand breaks by a mechanism involving free radicals and active oxygen species. These activities are enhanced by the ability of the quinone agent to alkylate DNA. L5178Y lymphoblastic cell lines resistant to quinone antitumor agents have been developed. These cell lines are 4- and 8-fold less sensitive to the non-alkylating quinone, HBM, than parent cells, are crossresistant to the alkylating quinone agent, BM, but show no resistance to AM, an alkylating agent that does not contain a quinone group. Both HBM and BM produce lower levels of DNA strand breaks in the resistant cells than in sensitive cells. In addition, DNA crosslinking by BM is reduced in the resistant cells; whereas, crosslinking by AM is unchanged. Earlier work has shown that the alkylating activity of BM is dependent on prior reduction of the quinone group. Since formation of free radicals by BM and HBM also requires reduction of the quinone group, the lowered levels of DSB produced by HBM and BM and the reduced cross-linking of BM in the resistant cells may be due to a diminished ability of these cells to reduce the quinone group.

THE CONTRIBUTION OF ALKYLATION TO THE ACTIVITY OF QUINONE ANTITUMOR AGENTS

Asher Begleiter and Marsha K. Keith

Studies have shown that the quinone group can produce tumor cell kill by a mechanism involving oxygen species. This cytotoxic activity can be correlated with the induction of DNA double strand breaks and is enhanced by the ability of the quinone compound to bind to DNA by alkylation. The cytotoxic activity and the production of DNA damage by model quinone antitumor agents were compared in L5178Y cells, sensitive and resistant to alkylating agents in order to assess the contribution of alkylation to the activity of these agents. The resistant, L5178Y/HN2, cells were found to be 2-fold and 6-fold more resistant to the alkylating quinones, benzoquinone mustard and benzoquinone dimustard, respectively than parent L5178Y cells. In contrast the L5178Y/HN2 cells showed no resistance to the non alkylating quinones, hydrolyzed benzoquinone mustard and bis(dimethylamino)benzoquinone. The alkylating quinones produced approximately 2-fold less crosslinking in L5178Y/HN2 cells compared to L5178Y sensitive cells. DNA double strand break formation by hydrolyzed benzoquinone mustard and bis(dimethylamino)benzoquinone was not significantly different in sensitive and resistant cells. However, the induction of double strand breaks by the alkylating quinones, benzoquinone mustard and benzoquinone dimustard was reduced by 5-fold and 15-fold respectively in L5178TY/HN2 cells. These results show that the alkylating activity of the alkylating quinones cannot directly explain all of the enhanced cytotoxic activity of these agents. Furthermore, they provide strong evidence that the enhanced formation of DNA

double strand breaks by alkylating quinone agents is directly related to the ability of these agents to bind to DNA. This increased formation of strand breaks may account for the enhanced cytotoxic activity of the alkylating quinones.

BIOCHEMICAL CHANGES IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) FOLLOWING TREATMENT WITH 2'-DEOXYCOFORMYCIN (DCF)

Asher Begleiter, Linda Pugh, Lyonel G. Israels and James B. Johnston

Two patients with refractory B-cell CLL were studied to examine the biochemical changes in CLL following treatment with the adenosine deaminase (ADA) inhibitor, DCF. Prior to therapy, the patient's peripheral lymphocytes were incubated *in vitro* for 24 hr with 1,5 or 50 μM deoxyadenosine (dAdo) and DCF (5 μM). The cellular deoxyATP concentrations were determined by a DNA polymerase assay and DNA single strand breaks (SSB) were measured by alkaline elution. The results were compared with those obtained using the peripheral lymphocytes from two normal individuals.

Subject	1 μM dAdo = DCF		5 μM dAdo = DCF		50 μM dAdo = DCF	
	dATP*	SSB**	dATP	SSB	dATP	SSB
Patient A	2.1±1.0	13±29	30.0±6.5	55±42	421.2±28.9	138±21
Patient B	0.6±0.5	0±30	12.0±1.3	0±32	64.7±14.0	18±60
Normal A	8.1±0.8	58±30	13.0±1.7	274±92	86.0±4.0	278±62
Normal B	2.0±0.4	117±24	7.2±0.9	200±85	50.0±4.0	379±110

*pmol/10^6 cells **rad equivalents

Patient A was treated with DCF, 4 mg/M^2 i.v. on a weekly basis, a regime that has been shown to be effective in some patients with this malignancy. The patient's peripheral lymphocyte ADA activity prior to therapy was 56 μM adenosine/hr/10^6 cells which was lower than that in normal peripheral mononuclear cells (range 70-200). The lymphocyte ADA activity was ablated 24 hr following treatment and returned to 25% of the pretreatment level at day 8. The cellular deoxyATP concentration increased from background levels to 8.8 ± 1.7 pmole/10^6 cells and 11.1 ± 3.4 pmol/10^6 cells 24 hr and 72 hr after treatment before returning to background levels at day 8. At these times there was no evidence of DNA SSB. The lymphocyte count did not change during the first 3 weeks of therapy suggesting that this patient is unresponsive to DCF. Patient B is awaiting treatment.

In summary, the formation of DNA SSB in lymphocytes incubated *in vitro* with dAdo and DCF does not correlate with the degree of accumulation of deoxyATP. Furthermore, these biochemical changes do not appear to be predictive of the clinical responsiveness of CLL patients to DCF.

ALTERATIONS IN MEMBRANE GLYCOPROTEINS DURING THE SENESCENCE OF NORMAL HUMAN DIPLOID FIBROBLASTS IN CULTURE

John A. Blondal, John E. Dick and Jim A. Wright

The plasma membrane is intimately involved in a variety of cellular phenomena and may play an important role in the aging of human cells in culture. Significant differences in human diploid fibroblast surface glycoproteins were observed with in vitro aging. Senescent cells bound more concanavalin A (Con A) than young cells and exhibited two distinct class

of binding sites. Cell surfaces of senescent cells incorporated less labelled mannose and more labelled fucose and glucosamine than young cell surfaces. Membranes prepared from older cells were also less effective than membrane preparations from young cells in incorporating mannose from GDP-mannose into a group of oligolipid intermediates, required for the synthesis of glycoproteins with asparagine-linked oligosaccharides. These results demonstrate novel quantitative changes in membrane structure and lectin reactivity in aging human diploid fibroblasts, which must reflect the fundamental physiological modifications in the cell that occur during senescence.

EVIDENCE THAT THE ANTIESTROGEN BINDING SITE IS A HISTAMINE OR HISTAMINE-LIKE RECEPTOR

Lorne J. Brandes, Linda M. Macdonald and R. Patricia Bogdanovic

N,N-diethyl-2-[(4 phenylmethyl)-phenoxyl]-ethanamine.HCl (DPPE), a compound selective for the antiestrogen binding site, is structurally similar to the aminoethyl ether group of antihistamines. Our studies now reveal that H_1-, but not H_2-antagonists, also compete for this site in the order: DPPE = hydroxyzine = prochlorperazine > phenyltoloxamine > pyrilamine > diphenydramine. The affinity of these compounds for the antiestrogen binding site correlates with their in vitro cytotoxicity against MCF-7 and EVSA-T human breast cancer cells. Tamoxifen, DPPE and hydroxyzine also bind to H_1 receptors present in digitonin-solubilized rat liver microsomes, but with less affinity than pyrilamine, which is selective for this site; the ratio of H_1 to antiestrogen binding sites in this preparation is 4:1. The data suggest that the antiestrogen binding site may be, in whole or in part, a receptor for histamine different from H_1 and H_2.

INVESTIGATION OF A NOVEL HISTAMINE BINDING SITE (H_3) IN BRAIN

Lorne J. Brandes

During the course of investigation into mechanism of action of antiestrogens, which are widely used in the treatment of hormonally-responsive breast cancer, we appear to have discovered a unique histamine binding site of apparent widespread distribution, which may be important to the mechanism of action not only of antiestrogens, but also of opiates, phenothiazines and tricyclic antidepressants. The discovery of this unique histamine binding site (H_3) was made possible by the synthesis (L. J. Brandes et al) of a novel compound, N,N-diethyl-2-[(4 phenylmethyl)-phenoxyl]-ethanamine HCl (DPPE), This structure of this compound strongly resembles that of known H_1 antagonists, but in binding studies using a custom labelled [^{3}H] DPPE compound we have demonstrated that DPPE binds to a unique site different from H_1 and H_2. Furthermore, preliminary investigations reveal that DPPE competes with [^{3}H] histamine for binding to histamine sites in rat cerebral cortex with an affinity apparently greater than either H_1- or H_2-antagonists. We also have demonstrated in this preparation the presence of reasonably high affinity saturable DPPE binding sites (50-150 fmol/mg protein); phenothiazine and tricyclic derivatives compete with varying degrees of affinity for [^{3}H] DPPE binding. Preliminary in vivo studies in Swiss Webster mice indicate that DPPE may be anxiolytic at concentrations which are not sedative; this contrasts with the H_1 antagonist pyrilamine which appears to cause mainly sedation. In the same strain of mice, DPPE at a concentration of 32 mg/kg almost completely prevents naloxone-precipitated morphine withdrawal leaping. Previous studies with H_1-antagonists

show that they increase morphine withdrawal leaping, while H_2-antagonists have only a mild ameliorating affect. Further binding studies show no evidence for direct interaction of DPPE with the opioid receptor, since naloxone does not compete with [^{3}H] DPPE for binding to the DPPE site and vise versa. We suggest a model common both to antiestrogens and to opioids in which histamine release occurs as a result of binding of the natural ligand to its specific receptor with H then acting through an associated H_3 binding site; DPPE may block both systems by antagonizing the H_3 binding site and not by any direct interaction with the primary receptor. The discovery of a unique binding site for histamine through the synthesis of an apparently selective antagonist for this site (DPPE) represents a unique opportunity to study novel mechanisms whereby histamine may function as a neurotransmitter or neuromodulator. Clarification of the mechanism of action of DPPE may lead to completely new concepts of the pharmacology of opiates, phenothiazines and other psychotropic drugs, all of which could be acting, in part, through an associated histamine binding site different from H_1 and H_2.

CHARACTERIZATION OF TUMOR PROGRESSION FROM THRESHOLD TUMOR INOCULA: EVIDENCE FOR NATURAL RESISTANCE

Garth W. Brown and Donna A. Chow

An examination of the variant generation and selection hypothesis of tumor progression was undertaken using the NK-sensitive, NAb-sensitive SL2-5 lymphoma in the threshold inoculum model of tumor progression. Tumor cells obtained from the i.p. injection site expressed heterogeneity for sensitivity to syngeneic NAb and to NR measured in the ^{131}IUdR-labelled tumor elimination assay. Cells retrieved from the s.c. injection site exhibited reductions in sensitivity to NR which correlated with decreases in sensitivity to syngeneic NAb and NK cells in vitro. These data confirm and extend our previous observations with the NK-resistant L5178Y-F9 lymphoma and further substantiate the evidence for the participation of NAb and NK cells in host-mediated antitumor resistance. Characterization of the model revealed that the selection for reduced sensitivity to NR in thymus-depleted AT x BM mice and normal animals could not be distinguished, suggesting that thymus-independent mechanisms may be major contributors to the surveillance of nascent tumors. The decreases in susceptibility to NR occurred in a stepwise and time-dependent manner in accord with the sequential multistage concept of progression. Furthermore, the selection for tumor cells which exhibited reductions in sensitivity to NR correlated with selection for increased tumorigenicity, in keeping with the idea that progression is associated with development towards an increasingly autonomous tumor.

RIBONUCLEOTIDE REDUCTASE ACTIVITY IN NORMAL HUMAN DIPLOID FIBROBLASTS IN CULTURE

John E. Dick and Jim A. Wright

Changes in ribonucleotide reductase occur during the senescence of normal human diploid fibroblasts in culture. Enzyme activity is significantly lower in cells and extracts at high mean population doublings (MPD) as compared to fibroblasts at low MPD. Although many of the kinetic properties of the enzyme remain unaltered in cells at high MPD, changes in the extent and kinetic mechanism of inhibition of CDP and ADP reductase activity by dATP, the

overall negative effector of ribonucleotide reductase, were observed. These results suggest that there is a link between ribonucleotide reduction, deoxyribonucleotide pools, and the establishment of the non-proliferative or senescent state.

DEOXYRIBONUCLEOTIDE POOLS IN HUMAN DIPLOID FIBROBLASTS

John E. Dick and Jim A. Wright

Since very little information about the levels of deoxyribonucleotide pools in human cells is currently availabled, an analysis of these pools was carried out with normal human diploid fibroblasts at various stages of senescence. These studies indicated that there are marked age-related perturbation in deoxyribonucleotide concentrations. It is suggested that these changes in pool sizes may be fundamentally related to the finite proliferative abilities of cultured human diploid fibroblasts. When one or more of these specialized compounds of DNA synthesis decline below a critical threshold level required for DNA synthesis, the cells would lose their proliferative characteristics. For example, the control of cell cycle progression which is closely related to the process of senescence has been described in terms of stochastic or random transition models. In these models, the initiation of DNA synthesis is governed by the probability that a small number of initiation factors will rise above a critical threshold concentration, and the synthesis of DNA will begin. If these factors are not elevated above this threshold, the probability of cell cycle progression remains very low. We suggest that the deoxyribonucleotides may belong to this select group of initiators of DNA synthesis, however, further studies are required to test this hypothesis.

IN SITU HYBRIDIZATION TO THE RAT DORSOLATERAL PROSTATE

J. G. Dodd, R. Sweetland, P. C. Sheppard and R. J. Matusik

In situ cDNA-mRNA hybridization histochemistry has been used to localize two nucleic acid sequences within the rat dorsolateral prostate. Clones corresponding to an androgen inducible RWB gene, and an androgen plus zinc regulated M-40 gene(s) were examined. The RWB gene codes for a secreted protein identified as SVS II while the M-40 gene(s) corresponds to two proteins (J. Dodd et al, JBC 258, 10731, 1983). Initial *in situ* hybridization utilized P^{32}-labelled DNA clones. Both RWB and M-40 mRNA localize within the lateral (L) lobe. Isolated mRNA measurements indicated that both genes were expressed about 5-fold higher in the L lobe versus dorsal lobe. After castration, the RWB mRNA decreased in L lobe whereas isolated areas continued to express M-40 mRNAs at high levels. The high content of zinc (10-fold higher than any other tissue) in the L lobe may account for this continued expression of the M-40 gene(s). In order to examine specific cell populations, biotin-labelled cloned DNA was detected by immunohistochemical techniques. Ultimate cellular location was determined by fluorescence. Within the L lobe, two distinct histological morphology types became apparent. Some acini are highly involuted and often contain cellular material within their lumen while other acini contain a minimal involution with thinner epithelium. After castration, the RWB expression decreased in both types while M-40 expression decreased primarily in acini associated with the thinner epithelium. For both mRNAs, fluorescence was confined to the area surrounding the nucleus — corresponding to the site of the endoplasmic reticulum. Surprisingly, even after castration, the involuted regions not only expressed M-40 mRNAs but also maintained normal cellular activity.

However, the RWB gene within these epithelial cells was de-induced in the absence of androgens. Thus, their continued cellular activity in the absence of androgens (rather than atrophy) indicates some "cellular promotors" beyond the control of androgens.

H-RAS TRANSCRIPTIONAL ACTIVATION AND METASTASIS FORMATION

Sean E. Egan, Grant A. McClarty, Jim A. Wright, I. Spiro, G. Hager and Arnold H. Greenberg

It has been shown that NIH/3T3 transfected with T24 *H-ras* are capable of forming experimental and spontaneous metastases in nu/nu mice. In our study, C3H 10½ mouse cells were transfected with T24 *H-ras* inserted into pSVneo, and selected in G418 sulphate. G418-resistant colonies were picked with both refractile and flat morphology. The morphologically transformed colonies gave rise to highly tumorigenic and metastatic lines (in nu/nu and C3H mice), whereas the phenotypically flat NR3 cell line was poorly tumorigenic and produced only rare experimental lung metastases.

Southern blot analysis revealed the presence of novel *H-ras* sequences in all five transfectants, however there was no correlation between gene copy number and metastasis formation. Examining the level of *H-ras* expression we found a strong correlation with metastatic efficiency. Four individual lung tumors derived from the poorly expressing NR3 were isolated, and expressed high levels of *H-ras* RNA and were highly metastatic. These four metastases show evidence of gene amplification and rearrangement.

Line 433 is an NIH-3T3 line containing a plasmid in which the H-MSV p21 gene is transcriptionally regulated by the glucocorticoid sensitive MMTV-LTR. Dexamethasone induction of p21 expression resulted in a 2.5 to 3-fold increase in experimental metastasis formation.

These results indicate that increased expression of activated *H-ras* sequences in both 10T½ and NIH-3T3 cells can result in enhanced metastatic potential. Furthermore, lung colonization by *H-ras* transfected 10T½ preferentially selects for transcriptionally enhanced variants.

MYC EXPRESSION IN hBPH AND CaP

W. H. Fleming, A. Hamel, R. MacDonald, E. Ramsey, N. M. Pettigrew, B. Johnston, J. G. Dodd and R. J. Matusik

Chromosomal abnormalities are often consistent in many cancers. The most common defects are band deletion or reciprocal translocation between two chromosomes. Although detailed chromosome analyses of human prostatic cancer is laccking, cytogenetic information on prostatic cancer (CaP) cell lines have revealed chromosome abnormalities. If non-random chromosome changes do occur, they may be related to oncogene expression. The specific translocation and activation of the myc oncogene in Burkitt lymphoma has been well documented. The association of myc expression with cell division in culture and in cancer has been studied. However, expression in benign tissue has not been examined previously. We report here preliminary data on myc levels in normal, BPH and CaP tissues. Northern analysis of isolated mRNA reveals the presence of myc mRNA (2400 nucleotides). The myc level in one CaP sample was assigned to the 100% and all other samples were normalized to that value. Expression in normal human prostates was low: 2.2% (22 yr old) and 4.3% (67 yr old). The myc levels in 10 patients with BPH ranged from 7.1% to 75% with an eleventh individual at 257%; while in 7 patients with CaP the myc levels ranged from 25%

to 100%. Relative to RNA isolated from human HL-60 cells (a promyelocytic line with amplified myc genes), the highest human CaP was approximately 14-fold lower. These data suggest that myc expression is higher in most human BPH and CaP tissue compared to normal prostatic tissue. Additional samples are now under analysis. The data indicate that myc expression does not directly correlate with malignant histology since myc is elevated in BPH which remains in a localized disease.

In cell culture systems, myc expression does correlate with cell division. Its expression in BPH may represent this event. At this time it is not possible to ascertain if myc expression is a cause or a consequence of prostatic diseases.

THE EFFECTS OF 1-OLEOYL-2-ACETYLGLYCEROL ON PLATELET PROTEIN PHOSPHORYLATION AND PLATELET ULTRASTRUCTURE

Laura L. Friesen, Jon M. Gerrard

1-oleoyl-2-acetylglycerol (OAG), an activator of protein kinase C and a synthetic diglyceride, was used in an investigation of the role of diglycerides in platelet stimulus-activation coupling. OAG (20-100 μg/ml) added to platelets resulted in rapid phosphorylation of the 47,000 dalton protein as well as gradual dose dependent disappearance of alpha granules and dense bodies and the appearance of vacuolar structures containing remnants of granule matrix material. These morphologic changes occurred more slowly than the phosphorylation of 47K, which suggests that if these are related the phosphorylated 47K serves to activate some other mechanism, which is ultimately responsible for the changes observed. These results are most consistent with a role for the phosphorylation of 47K to promote granule labilization. Myosin light chain (MLC) phosphorylation also occurred. An absence of granule centralization suggests that MLC phosphorylation by protein kinase C may not trigger effective actin-myosin contraction.

PROTEIN PHOSPHORYLATION AND PLATELET SECRETION

Jon Gerrard, Laura Friesen

Platelet secretion in response to physiologic stimuli appears to result from the complementary stimulation of two processes — granule centralization and granule membrane fusion. Granule centralization is produced by actin-myosin contraction which is initiated by a movement of calcium ions into the cytoplasm. The calcium binds to calmodulin to form a complex which activates myosin light chain kinase to phosphorylate myosin light chain (MLC). Once phosphorylated in this fashion, actin-myosin contraction occurs. Granule membrane fusion can be produced selectively by phorbol myristate acetate and oleoyl-acetyl diglyceride, both of which activate protein kinase C. Phosphorylation of a 47,000 dalton intracellular protein (47K) by protein kinase C may be critical to granule membrane fusion. The mechanism of action of 47K is presently unknown. The combined phosphorylation of MLC and 47K in response to most physiologic agonists which cause granule secretion, and the synergistic effects on granule secretion of agents which independently stimulate MLC and 47K phosphorylation, suggests secretion usually results from the interaction of granule centralization and granule membrane fusion.

COOPERATIVE TRIAL OF IMMUNOTHERAPY FOR NASOPHARYNGEAL CARCINOMA WITH TRANSFER FACTOR FROM DONORS WITH EPSTEIN-BARR VIRUS ANTIBODY ACTIVITY

Gerald J. Goldenberg, Lorne J. Brandes, W. H. Lau, A. B. Miller, Claus Wall and John H. C. Ho

A prospectively randomized, double-blind clinical trial was conducted to evaluate the effect of immunotherapy with transfer factor (TF) as an adjunct to radiotherapy of patients with stage III nasopharyngeal carcinoma (NPC). The TF was derived from normal young adults with a proven history of infectious mononucleosis and from normal blood donors with elevated antiviral capsid antigen antibody activity. TF prepared in this fashion was previously shown to convert the leukocytes of patients with NPC to a relative state in vitro and when administered to NPC patients in vivo was associated with apparent slowing of tumor growth, marked lymphocytic infiltration of the tumor, and reconstitution of delayed cutaneous hypersensitivity reactions. From 1974 to 1977, 100 patients with NPC were entered in the study; one-half of the patients were treated with radiotherapy alone and one-half received radiotherapy and an 18-month course of TF immunotherapy. The patients were followed for at least 5 years. No significant difference in disease-free survival or survival was noted between the two groups of patients. The use of this particular preparation and dose schedule of TF in patients with NPC with regional disease was devoid of any antitumor activity.

INDUCTION OF DNA SINGLE- AND DOUBLE STRAND BREAKS BY DIETHYLSTILBESTROL IN MURINE L5178Y LYMPHOBLASTS IN VITRO

Gerald J. Goldenberg and Evelyn K. Froese

The mechanism of action of the synthetic estrogen diethylstilbestrol (DES) was investigated in murine L5178Y lymphoblasts. The dose-survival curve of cells treated with DES in serum-free medium for 1 hr was characterized by a prominent shoulder followed by a simple exponential decline; the D_0, the dose of DES reducing cell survival to 1/e, was 1.52 nmoles/ml. DNA single-strand breaks, as measured by the alkaline elution method, was observed in DES-treated cells, and these followed a dose-response relationship after an apparent threshold of 10 μM DES was exceeded. Protein-associated strand breaks, which represent the increment in single-strand breaks that occurs by exposing drug-treated cells to proteinase K, were also noted. DNA double-strand breaks as measured by filter elution technology at pH 9.6 were observed and increased markedly to reach a level of approximately 9000 rad equivalents at a DES concentration of 20 μM. The measured ratio (mean $\pm$ S.E.) of single- to double-strand breaks induced by DES in L5178Y lymphoblasts was 0.09 ± 0.035. A comparison of the ratio of single- to double-strand breaks induced by DES to that observed following radiation suggested that all of the single-strand breaks produced by DES could be attributed to double-strand breaks. The close correspondence of the dose-response curve for cytocidal activity of DES with that obtained for induction of DNA double-strand breaks suggested that such breaks may play an important role in the mechanism of cell kill by DES.

ANTAGONISM OF THE CYTOCIDAL ACTIVITY AND UPTAKE OF MELPHALAN BY TAMOXIFEN IN HUMAN BREAST CANCER CELLS IN VITRO

Gerald J. Goldenberg and Evelyn K. Froese

The effect of the antiestrogen tamoxifen on the cytocidal activity and uptake of melphalan in human breast cancer cells was investigated. A clonogenic assay was used to obtain dose-survival curves of estrogen receptor-positive MCF-7 cells and of estrogen receptor-negative Evsa T cells following treatment with melphalan and/or tamoxifen. Isobolograms derived from these dose-survival curves were concave downward, suggesting that the drug interaction was antagonistic. The effect of tamoxifen on melphalan uptake by breast cancer cells was evaluated at steady-state conditions. Thin-layer chromatography revealed that the intracellular level of free intact melphalan (mean $\pm$ S.E.) in control cells was 6.47 ± 1.21 fmoles/cell and that in cells treated with tamoxifen was 3.60 ± 0.35 fmoles/cell; this 44% reduction in cellular melphalan was statistically significant ($p = 0.006$). Thus, the antagonistic cytocidal effect of melphalan and tamoxifen against breast cancer cells appeared to be due to inhibition of melphalan uptake at the steady state by the antiestrogen. Further investigation revealed that tamoxifen inhibited unidirectional melphalan influx in human breast cancer cells both by the sodium-independent system L and by the sodium-dependent system ASC. Tamoxifen also appeared to stimulate melphalan efflux from human breast cancer cells. The first-order rate constant K for melphalan efflux from control cells was 0.085 ± 0.008 and that from cells treated with tamoxifen was 0.129 ± 0.005; the difference was highly significant ($p < 0.001$). Therefore, the antagonistic effect of tamoxifen on the uptake and cytocidal activity of melphalan in breast cancer cells appeared to be due to inhibition of melphalan influex and stimuiation of drug efflux.

ACTIVATION OF LOBSTER HEMOCYTES: CYTOARCHITECTURAL ASPECTS

P. Z. Goldenberg, A. H. Greenberg, J. M. Gerrard & E. Huebner

Activation for the phagocytosis of erythrocytes following the attachment of lobster (*Homarus americanus*) hemocytes to an underlying substrate has been demonstrated in earlier experiments. Morphological evaluation of hemocytes during the activation period by scanning electron microscopy (SEM) revealed progressive changes from spherical, smooth-membraned cells to 'activated' hemocytes bearing filopodia, broad lamellopodia and a flattened cell soma. Microfilaments within filopodia were observed by transmission electron microscopy (TEM). The rate of hemocyte membrane changes was uneven over the activation period producing a full range of morphological types after 6 hours in culture. This diversity may be a reflection of cell motility or the presence of heterogeneous hemocyte populations. At least two cell types could be identified by (Nomarski) differential interference microscopy after activation, granulocytes and hyalinocytes, distinguished by the presence or absence of cytoplasmic granules. Alterations in these cytoplasmic granules during activation were noted by TEM. The striated cytoplasmic granules found in fresh hemocytes disappeared within 6 hours leaving only electron dense granules. Additional TEM changes including vacuolation, the development of a heterochromatic nucleus and the appearance of electron lucid extracellular material were consistently associated with the activation process. When sheep erythrocytes were added to activated hemocyte cultures, they could be detected within phagosomes, attached to filopodia and enfoiled by lamallae at the cell surface. In general,

hemocytes were observed to share functional and morphological features with mammalian cells, in particular macrophages and platelets. The similarities observed are in accord with the hypothesis that the circulating hemocytes of diverse phyla evolved from a common ancestor.

ACTIVATION OF RAT AND HUMAN ALVEOLAR MACROPHAGE INTRACELLULAR MICROBICIDAL ACTIVITY BY A PREFORMED LGL CYTOKINE

Jose Gomez, Bill Pohajdak, Shane O'Neill, John Wilkins and Arnold H. Greenberg

An alveolar macrophage-activating factor was released from Percoll fractionated large granular lymphocytes (LGL) within minutes of contact with either the natural killer (NK)-sensitive K562 tumor or heat-killed *Staphylococcus aureus*. The factor enhanced the intracellular killer of S. aureus without altering the rate of phagocytosis. Factor release was blocked by treatment of LGL with momensin, a carboxylic ionophore that inhibits vesicular traffic, but was unaffected by actinomicin D and cycloheximide pretreatment, suggesting that the cytokine was preformed. The cell producing the factor was found only in Percoll fractions containing high concentrations of lytic NK cells and LGL, and the phenotypes of the LGL were HNK-1^+ and E rosette negative. The macrophage activating factor was a small protein of 10,000 to 20,000 daltons, as determined by gel fractionation, and was sensitive to proteolytic enzymes and heat and pH labile. Active supernatants were devoid of antiviral (interferon; IFN) or interleukin (IL 2) activity, and IFN-β, IFN-γ, IL 2, and interleukin 1 were unable to activate staphylococcidal activity, suggesting that the LGL macrohage activating factor was distinguishable from these cytokines.

GENETIC REGULATION OF NATURAL ANTI-TUMOR ANTIBODIES: THE ROLE OF H-2 AND X-LINKED GENES

Arnold H. Greenberg and Donna A. Chow

Although natural anti-tumor antibody (NAb) has been detected against an impressive number of different tumors in several species, as well as within most inbred strains of mice, this reactivity is not uniform. Studies of tumor panels have consistently revealed high and low reactivity in sera of given strains to specific tumors, and sera from individual strains vary in reactivity to a number of different tumors. This dependency on the strain-tumor combination to detect NAb is consistent with both a genetic regulation of NAb production, in which high and lower producer strains exist for a single tumor, as well as a wide range of antigenic variation among tumors so that different NAb specificities within a given strain may be detected. Using cloned murine tumors, we observed that NAb levels were dependent on the strain-tumor combination, and that high NAb levels were inherited recessively. Natural antibody to one murine lymphoma was regulated by genes closely linked to the H-2 locus of the d haplotype. X-linked genes in the B cell deficient CBA/N mice could suppress NAb production and complementation with the $H\text{-}2^d$ gene was sufficient to totally suppress NAb levels and make the mice unresponsive to polyclonal B cell activation by lipopolysaccharide.

ACTIVATION OF PERMEABILIZED PLATELET BY INOSITOL-1,4,5-TRISPHOSPHATE

Sara Israels, Pauline Robinson, Jon Gerrard, John C. Docherty

The effect of inositol-1,4,5-triphosphate (IP_3) was studied using human platelets permeabilized with saponin and suspended in a high potassium Ca^{2+}-free buffer containing 40 μM EGTA and 1.2 mM magnesium. Under these conditions IP^3stimulated aggregation at a concentration of 0.5 μM with maximum aggregation at 5.0 μM. Aggregation was associated with phosphorylation of myosin light chain and a 47,000 dalton protein, and with a change in platelet shape including granule centralization and pseudopod formation similar to changes seen when cytoplasmic calcium is raised by other means. IP^3 stimulated [^{14}C]-serotin release from platelet dense granules, [^{14}C]-arachidonic acid release from platelet phospholipids and production of thromboxane B^2. Preincubation of platelets with aspirin which blocked thromboxane formation also inhibited protein phosphorylation, serotonin secretion and partially inhibited aggregation. These results support the concept that IP^3 is a major intracellular messenger in platelets and suggests that its effects are mediated both through Ca^{2+} flux and thromboxane formation.

BIOCHEMICAL CHANGES INDUCED IN HAIRY-CELL LEUKEMIA FOLLOWING TREATMENT WITH THE ADENOSINE DEAMINASE INHIBITOR 2'-DEOXYCOFORMYCIN

James B. Johnston, Asher Begleiter, Linda Pugh, Marsha K. Leith, John A. Wilkins, Douglas J. Cavers, and Lyonel G. Israels

The adenosine deaminase inhibitor 2'-deoxycoformycin and interferon are highly effective in the treatment of hairy-cell leukemia. In this study, a patient with Type II hairy-cell leukemia was treated with one cycle of 2'-deoxycoformycin (4 mg/M^2, i.v. weekly x 3), which was repeated at 9 weeks. No toxicity was observed and the hairy cell count fell from 72,000/mm^3 to 5,000/mm^3 in three months, with a concomitant 50% decrease in the spleen. The erythrocyte deoxyATP content increased to 13.6 pmol/10^6 cells following the initial 3 weekly treatments, but there was no decrease in the ATP pool size and no evidence of hemolysis. The hairy cell adenosine deaminase activity was inhibited by $>$ 95% 24 hr following the first 2'-deoxycoformycin injection and returned to the pretreatment value at day 8, although there was a linear decline in peripheral hair cell count (50%) during this period. No ultrastructural changes were observed in the hairy cells following 2'-deoxycoformycin to suggest lymphocytotoxicity, or cellular differentiation. The antitumor activity of 2'-deoxycoformycin could not be attributed to alterations in the hairy cell deoxyATP/ATP levels, or to the induction of DNA strand breaks. Additionally, the plasma levels of interferon did not change during therapy making it unlikely that 2'-deoxycoformcin exerts its activity by inducing endogenous interferon synthesis.

EVIDENCE THAT TAMOXIFEN IS A HISTAMINE ANTAGONIST

Edwin A. Kroeger and Lorne J. Brandes

Recently we reported that both the triphenylethylene antiestrogen tamoxifen, and the novel compound N,N-diethyl-2-[(4 phenylmethyl)-phenoxy]-ethanamine.HCl (DPPE), which is selective for the antiestrogen binding site, may be histamine antagonists and have suggested

that the antiestrogen binding site may be a growth-promoting histamine receptor different from H_1 and H_2 (H_3). We now show that alone with established H_1-antagonists, tamoxifen and DPPE specifically block the histamine-induced (H_1) contraction of canine trachael smooth muscle in the order: pyrilamine = hydroxyzine > tamoxifen = 4-hydroxytamofixen > DPPE. The H_1-antagonist hydroxyzine, which competes about equally with DPPE for the antiestrogen binding site, is up to 10^3 times stronger than DPPE in blocking histamine-induced muscle contraction. This shows that H_1 antagonism is distinct from binding to the antiestrogen binding site and suggests that if the latter is a histamine receptor, it is not H_1; presumably tamoxifen and DPPE compete for this novel site in addition to, and with greater affinity than, H_1.

DEVELOPMENT AND CHARACTERIZATION OF MONOCLONAL ANTIBODIES OF BOVINE BRAIN CALCINEURIN

Hing-Yat Peter Lam

Calcineurin, a major calmodulin binding protein in brain, was discovered originally as an inhibitor of calcium-calmodulin dependent phosphodiesterase. It is a heterodimer composed of a 60,000 Mr calmodulin binding subunit (α) and a 19,000 Mr subunit (β) capable of binding four Ca^{2+}. Recently, calcineurin was shown to be a phosphoprotein phosphatase. Its substrates include several artificial and endogenous phosphoseryl-,phosphothreonyl- and phosphotyrosyl proteins, p-nitrophenyl phosphate, phosphoenolpyruvate and phosphotyrosine. Though the physiological function of this phosphatase has not been elucidated, its role in the regulation of neurotransmitter action and microtubular function was suggested by some investigators. More recently, it has been shown that calcineurin can dephosphorylate the phosphotyrosyl group on the epidermal growth factor receptor and implication of this phosphatase in cell growth regulation and cell transformation has been suggested. We have purified human brain calcineurin to homogeneity and developed monoclonal antibodies against bovine brain calcineurin. These antibodies were shown to cross-react with calcineurins isolated from different species including human, rat and mouse. Study of the biochemistry of calcineurin by using these antibodies as probes is in progress.

DEMONSTRATION OF DIFFERENT METAL ION-INDUCED CALCINEURIN CONFORMATIONS USING A MONOCLONAL ANTIBODY

Hideki Matsui, Catherine J. Pallen, Anne-Marie Adachi, Jerry H. Wang and Peter H-Y. Lam

It has been suggested that calcineurin, a calmodulin-stimulated phosphatase, may exist in different metal ion-dependent conformational states (Pallen, C. J. and Wang, J. H. (1984) J. Biol. Chem. 259, 6134-6141). Evidence in favor of this hypothesis comes from studies involving a monoclonal antibody, VA_1, which is specific for the small (β) subunit of calcineurin. This antibody inhibits Ni^{2+}-stimulated but not Mn^{2+}-stimulated phosphatase activity against p-nitrophenyl phosphatasse and phosphorylase kinase. Inhibition is not due to competition of the antibody with substrate or to interference with metal ion binding to the enzyme. Complex formation between the antibody and calcineurin can be demonstrated either in the presence of Mn^{2+} or Ni^{2+} or in absence of metal ion activators. These results indicate that the active conformational states of calcineurin are metal ion dependent, that the monoclonal antibody VA_1 affects the Ni^{2+}-induced conformational change of the enzyme,

and that the β subunit of calcineurin plays a critical role in the expression of Ni^{2+}-stimulated phosphatase activity.

ANDROGEN REGULATION OF PROSTATIC GENES

R. J. Matusik, P. McNicol, R. Sweetland, C. Mullin, W. H. Fleming and J. G. Dodd

The rat prostate has been used as a model system to study androgen action. Most researchers have studied the ventral (V) lobes and its major secretory product "prostatic binding protein". Genes corresponding to three subunits of this protein have been cloned (Parker et al, JBC 255, 6996, 1980). Direct binding of purified androgen receptor to the a genomic clone has determined that specific binding sites exist at the 5' end and within the first intron (Perry et al, In: Regulation of Androgen Action, in press).

Since the rat dorsolateral (DL) and its equivalent counterpart, posterior, in the human are the site of prostatic cancer, we decided to focus our attention on these lobes. In vitro DL mRNA translation reveals four distinct proteins. These peptides comprise at least 35% of the DL protein synthesis. We have cloned the mRNAs for the 52 KDa (RWB) protein and a doublet of 23 and 21 KDa (M-40). The 52 and 23 KDa are microsome processed to 49 and 21 KDa, respectively. Thus, the presence of a signal peptide indicates secretion or membrane localization. The 52 KDa protein has been identified as the SVS II protein present in the seminal vesicles. Hybrid arrest translation indicates that a single M-40 cDNA clone will block the synthesis of both the 23 and 21 KDa proteins. Thus the only difference between this doublet may be the presence of a signal peptide. During DL prostatic maturation (3 to 6 weeks) expression of RWB and M-40 genes coincides with androgen production. However, the M-40 mRNAs undergo a developmental switch being expressed by the immature 3-week V prostate, suppressed to low levels in the 6-week V prostate and expressed by the 6-week DL prostate. The RWB mRNA is undetectable in the V lobe. Both the RWB and M-40 mRNAs are decreased in the DL after castration and stimulated by androgen therapy. Interestingly, the ventral M-40 gene does not respond to androgen withdrawal or stimulation. Rather, it appears to be constitutively expressed. Since the DL lobe concentrates zinc at levels higher than any other tissue, we decided to examine the role of zinc on gene expression. After androgen withdrawal (castration) the RWB expression is not reinduced by zinc alone. However, the M-40 expression can reach normal levels after zinc administration. We have confirmed that the M-40 gene does *not* correspond to a metallothionein. We are currently performing nuclear run off experiments to determine if androgen and zinc stimulate gene transcription.

In order to explore the deelopmental pattern of cellular differentiation these specific cDNA clones have been used for *in situ* cDNA-mRNA hybridization histochemistry. This information can compliment hybridization data obtained from total tissue homogenates such that an overall change in expression by all cells can be distinguished from a change in expresion by a few cells. Both RWB and M-40 mRNA localize within the lateral tip of the DL prostate. After castration, the RWB mRNA decreased whereas isolated areas continued to express the M-40 mRNA's at high levels. Epithelial cells that continued to express M-40 maintained normal cellular morphology. Since the RWB gene within these epithelial cells was de-induced in the absence of androgens yet these cells continued to be active in the absence of androgens (rather than atrophy), it indicates some "cellular promotors" beyond the control of androgens.

ALTERED RIBONUCLEOTIDE REDUCTASE ACTIVITY IN DRUG RESISTANT CELLS

G. McClarty, A. Chan and J. Wright

Ribonucleotide reductase catalyzes the reaction in which ribonucleotides are reduced to deoxyribonucleotides, the precursors for DNA synthesis. We have described the results from experiments with mouse L cells with 30 fold increase in resistance to hydroxyurea. Hydroxyurea is a potent inhibitor of ribonucleotide reductase. This resistant cell line (designated LHF) was selected by growing the parental line (L_{60}) in the presence of stepwise increasing concentrations of hydroxyurea. The hydroxyurea resistant phenotype was stable for at least 40 passages in the absence of the drug. However, when LHF cells were grown in the absence of hydroxyurea, their level of enzyme activity was greatly reduced. It appears that hydroxyurea can highly induce the enzyme activity in LHF cells. Enzyme activity in permeabilized LHF cell was 20 fold higher than that in L_{60} cells. Immunoprecipitation by rabbit antiserum against the M_1 subunit indicated that there was an overproduction of the M_1 subunit in the LHF cells. It is now well established that an important mechanism of drug resistance in cultured cells occurs through overproduction of enzyme activity by a process of gene amplification and at least in the case of methotrexate resistance this mechanism appears to play a role in clinical drug resistance situations. However, drug resistant cell lines which overproduce enzyme activity through qualitative changes in gene expression as opposed to quantitative changes in gene number are relatively rare. In this regard, the LHF cell line should be a valuable tool for investigating the expression of a key enzyme activity involved in DNA synthesis and cell proliferation. It also has the advantage that many conditional mutants have: cells cultured under one set of conditions (e.g. in the absence of hydroxyurea) provide an ideal control for experiments carried out with the same cell line after it has been placed under another set of conditions (e.g. cultured in the presence of drug). Furthermore, a mechanism involving an increase in enzyme activity on exposure to drug could have important clinical implications, and an elucidation of such a mechanism could lead to improved clinical protocols for drug treatment by manipulation of the intracellular enzyme activity. The availability of a cell line which expresses a drug-dependent increase in ribonucleotide reductase activity should be useful in studies aimed at gaining a better understanding of the regulation of this important enzyme activity *in vivo*, and this information could be relevant to problems in chemotherapy.

RIBONUCLEOTIDE REDUCTASE: AN INTRACELLULAR TARGET FOR THE MALE ANTIFERTILITY AND ANTIPROLIFERATIVE AGENT, GOSSYPOL

G. A. McClarty, A. K. Chan, D. C. Creasey and J. A. Wright

Gossypol is a yellow phenolic compound which reversibly inhibits spermatogenesis making it one of the few effective male antifertility drugs. The cytotoxic effects of gossypol have been associated with its ability to irreversibly inhibit DNA synthesis by a previously unknown mechanism. The results of this study indicate that gossypol is a potent inhibitor of ribonucleotide reductase the rate limiting enzyme activity in DNA synthesis. Furthermore, in agreement with these enzyme studies, DNA synthesis in a hydroxyurea resistant cell line with high levels of ribonucleotide reductase activity showed increased resistance to gossypol when compared to wild type cells with normal levels of reductase activity. Ribonucleotide

reductase is the first specific site of action documented for gossypol which can explain its recently described antiproliferative, cell cycle and toxic effects. It is worth noting that the prolonged use of antiproliferative agents in man may select for cells resistant to such agents. Therefore, extensive treatment with gossypol could effectively lead to the selection of drug resistant cells with increased ribonucleotide reductase activity. Due to the important regulatory role exhibited by the reductase in DNA synthesis and therefore cell proliferation, such variant cells may also have aberrant growth characteristics.

THE p53 CELLULAR ONCOGENE IN ERYTHROLEUKEMIA INDUCTION

M. Mowat, V. Chow, S. Benchimol and A. Bernstein

The objective of these studies is to determine the role the p53 oncogene plays in the multistage erythroleukemia induced by Friend leukemia virus. We have recently described several erythroleukemia cell lines with altered p53 expression (Mowat et al, Nature 314:633-636, 1985). Some of these cell lines do not express p53 whereas others express very high levels of a truncated form of the protein. Cell lines not expressing p53 show reduced tumor forming ability when compared to p53 expressing cell lines. Using a p53 cDNA probe, we have found alteration of the p53 gene in these cell lines. We have isolated cell lines from the same mouse that either express a normal p53 protein or do not express p53. To determine whether the p53 positive and p53 negative cell lines were the result of the same or different transformation events *in vivo*, we have utilized the integration sites of Friend murine leukemia virus (F-MuLV) as a unique clonal marker. Southern gel analysis indicates that the p53 positive and negative cell lines from the same mouse were not clonally related, suggesting that at least two independent transformation events had taken place in these mice. We have also molecularly cloned the normal p53 gene from an expressing cell line and a rearranged p53 gene from a non-expressing cell line. The rearranged p53 gene has undergone a 2Kb deletion resulting in loss of several p53 exons. Preliminary results show that F-MuLV was not the cause of this deletion.

ACTIVATION IN VIVO OF A MAJOR ANTISUPPRESSOR T-CELL PATHWAY IMMEDIATELY AFTER IMMUNIZATION

I. Its Regulation by I-A Gene Products

F. Paraskevas, S-T Lee, J. Maeba and C. S. David

It has previously been demonstrated that within 6 hr after immunogenic stimulation the serum of mice contains a unique form of immunogenic antigen which represents complexes of Ig and antigen. The complexes are known to be strongly cytophilic for $Ly2^+$ Ia^+ FcR^+ T cells and markedly enhance the IgG response. Anti-I-A treatment of mice suppresses the IgG antibody response and results in the generation of antigen specific T suppressor cells (Ts). Furthermore, anti-I-A treatment blocks the induction of the complexes and abolishes the enhancing effect the complexes exert on the IgG antibody response. The 6-hr cytophilic complexes were shown to block the function of Ts and allow a normal IgG response to take place; therefore, they act as mediators of a novel T-cell pathway called antisuppression. The blocking of the induction of the antisuppressor complexes by anti-I-A antibody was at least in part due to an effect on T cells. In conclusion, products of genes of the I-A subregion of the MHC control the activation early after immunization of a T-cell

pathway which is called antisuppression since its major function is interference with the expression of suppression. Its early induction (within 6 hr) suggests that antisuppression may play a pivotal role in determining between immunity and unresponsiveness.

ACTIVATION IN VIVO OF A MAJOR ANTISUPPRESSOR T-CELL PATHWAY IMMEDIATELY AFTER IMMUNIZATION

II. T-Cell Requirements for its Expression

S-T Lee, F. Paraskevas and J. Maeba

Immunogens activate in vivo within 3-6 hr after injection a new and hitherto unrecognized T-cell pathway which interferes with T-cell suppression, therefore called antisuppression. An important soluble mediator with antisuppressor activity is detected in the serum of immunized animals within 3-6 hr. The mediator represents a unique form of complexes of Ig and antigen. The antisuppressor function of the complexes does not represent a direct "neutralizing" effect of the complexes on the effector T suppressor cells. The antisuppressor complexes activate an $Ly2^+$ T cell which, with the interaction of an $Lyl23^+$ T cell, blocks completely T-suppressor-cell function. The biological significance of the T antisuppressor pathway is discussed.

ACTIVATION IN VIVO OF A MAJOR ANTISUPPRESSOR T-CELL PATHWAY IMMEDIATELY AFTER IMMUNIZATION

III. T-Cell Requirements for its Induction

F. Paraskevas, S-T Lee and J. Maeba

Immunogenic stimuli rapidly induce a potent mediator with antisuppressor activity which represents complexes of Ig and antigen. The formation of the complexes depends on the interaction of two T cells both of which bear the Lyl phenotype. The two T cells can be separated on the basis of their sensitivity to antilymphocytic serum and dependency on the presence of thymus. T cells bearing I region coded determinants are essential for the formation of the mediator.

THE EFFECT OF GRAFT-VS-HOST REACTION (GVHR) ON THE ANTISUPPRESSOR T-CELL PATHWAY

S-T Lee, J. G. Gartner and F. Paraskevas

Permanent and profound immunosuppression is a well known complication of GVHR. The mechanism by which the graft suppresses the host is poorly understood. Previous studies have demonstrated that within 3-6 hrs, immunization activates a T-cell pathway with potent antisuppressor (Tαs) activity. Factors interfering with this pathway lead to immunosuppression. We therefore investigated the extent to which GVHR affects the induction and expression of the Tαs pathway as one possible mechanism leading to the immunosuppression seen during the reaction. We induced acute GVHR by I.V. injection of (C57BL/6xA/J) F_1-hybrids with $50x10^6$ A/J spleen and lymph node cells. Groups of mice with GVHR and control mice were immunized with sheep erythrocytes on days 8, 15 and 22 after induction of the reaction. Serum was collected 6 hrs after immunization (6HS). 6HS from normal mice contained a potent antisuppresor mediator. In contrast, in mice with GVHR the mediator

was no longer detectable by day 22 of the reaction. Expression of Tαs-pathway function depends on the interaction of the mediator with $Ly2^+$ cells. In a second experiment, we observed that T cells from mice undergoing a GVHR could not be activated by the mediator produced in normal mice. Those results suggest that GVHR has diverse effects on the Tαs-pathway, blocking both its induction and effector stage.

REGULATION OF ANTI-SUPPRESSION BY GENES OF THE Igh LOCUS

S. Unival and F. Paraskevas

Within 6 hr after immunogenic stimulation the serum of mice contains a unique form of immunogenic antigen which represents complexes of Ig and antigen ("6 hr complexes") and possess potent antisuppressor function. We present here evidence that their formation is Igh restricted. Sublethally irradiated mice are unable to produce "6 hr complexes" but do so only when reconstituted with syngeneic T cells. However, when CB.20 ($H\text{-}2^d$, $Igh\text{-}1^b$) mice are reconstituted with T cells from Balb/c ($H\text{-}2^d$, $Igh\text{-}1^a$) mice "6 hr complexes" are not generated. Addition of trace amounts of IgG from Balb/c mice as well as IgG from other strains possessing the $Igh\text{-}1^a$ haplotype allows generation of complexes. Immunoglobulin G from BAB.14 ($Igh\text{-}V^a$, $Igh\text{-}C^b$) mice was also effective. In the reverse experiment when Balb/c are reconstituted with CB.20 T cells, only IgG from $Igh\text{-}1^b$ haplotypes was effective while BAB.14 Ig ws not effective. Similar results have been obtained with the combination of Cal.20 ($H\text{-}2^d$, $Igh\text{-}1^d$) and Balb/c or CB.20 mice. In conclusion, we postulate that in the presence of MHC compatibility the complete complex is generated only if the IgG is derived from the donor of the T cells or strains with the same Igh haplotype as the T cell donor. Furthermore the heavy chain variable region is the restricting element in the formation of the "6 hr complexes".

REGULATION OF ANTISUPPRESSION BY CYCLOPHOSPHAMIDE SENSITIVE T CELLS

F. Paraskevas, S-T Lee and J. Maeba

Immunization activates within 3-6 hrs a potent T cell antisuppressor pathway (T s) which allows for a marked enhancement of the IgG antibody response. Cyclophosphamide (CY) also interferes with Ts function and enhances the IgG response. We have therefore examined the mechanism of action of CY in relation to Tαs.

Injection of Balb/c mice with 1-20 μg/kg of CY enhanced the IgG response to sheep erythrocytes (SRBC), especially for lower (10^6) doses. Serum collected 6 hrs after immunization (6HS) with SRBC, contains a potent antisuppressor mediator, which also enhances the IgG response to low doses of SRBC. While the CY induced enhancement is abolished with thymocytes or splenic Lyl^+ T cells, such reconstitution had no effect on the 6HS enhancement. Mice treated with CY generate the antisuppressor mediator to low doses of SRBC that are ineffective in normal mice and this effect is again abolished by Lyl^+ cells. Finally low doses of SRBC induce in the first 24 hrs an $Ly2^+$ Ts, but its induction is not affected by CY.

In conclusion, the enhancement of the anti-SRBC IgG antibody response by CY, is not due to a direct effect on the Ts pathway, but rather to the release from inhibition of the Tαs pathway, which in turn blocks Ts function.

B CELL DEPRIVED MICE LACK ANTI-SUPPRESSOR T CELL FUNCTION

J. Gordon, F. Paraskevas and S-T Lee

Previous work has identified selective defect(s) in T cells in mice deprived of B lymphocytes by the chronic administration of anti-IgM antibody. We have examined the ability of B cell deprived mice to activate a T cell antisuppressor pathway.

Mice were treated with anti-IgM from birth. Normally approximately 100% of splenic T cells possess Fc receptors and an equal number express Ia antigens detected by a sensitive rosetting technique. T cells from anti-IgM treated mice had no detectable Fc receptors nor surface Ia molecules. Normally within 6 hours after immunization a potent antisuppressor mediator is detected in the serum. Its generation and the expression of its function depend on Ia^+ T cells. In anti-IgM treated mice no mediator is generated and furthermore such mice lack the T cell subpopulation necessary for the expression of its function.

These results indicate that B lymphocytes are important for the development of a T cell pathway with potent antisuppressor activity.

THE ROLE OF PROSTAGLANDINS IN MEDIATING CHANGES IN MICROSOMAL ELECTRON TRANSPORT SYSTEM FUNCTION AND HEME OXYGENASE IN MURPHY-STURM LYMPHOSARCOMA-BEARING RATS

Brent A. Schacter and Mary Sauder

Previous studies by other investigators have suggested a possible inter-relationship between prostaglandin secretion by tumors and alterations in microsomal oxidative drug metabolism in tumor-bearing animals. During the past year, we have studied these inter-relationship in the Murphy-Sturm lymphosarcoma rat model and have made the following observations: (1) suspensions of dispersed Murphy-Sturm lymphosarcoma cells incubated with ^{3}H-arachidonic acid demonstrate significant formation of PGE_2, thromboxane B2, $FGF_{2\alpha}$, and 6-KETO $PGF_{1\alpha}$; (2) there is a dose-dependent decrease in 6-KETO $PGF_{1\alpha}$ synthesis by Murphy-Sturm lymphosarcoma cells incubated in the presence of increasing concentrations of indomethacin, an inhibitor of prostaglandin synthesis; (3) IP administration of indomethacin to control and tumor-bearing rats partially prevents the previously documented increase in hepatic heme oxygenase activity, but does not prevent the previously documented decreases in hepatic cytochrome P-450 concentration and NADPH-cytochrome *c* reductase activity; (4) ASA, a cyclo-oxygenase inhibitor, when administered to tumor-bearing rats produced a decrease in hepatic heme oxygenase but had no readily discernible effect on cytochrome P-450 or NADPH-cytochrome *c* reductase activity; (5) 16,16-dimethyl PGE_2 and PGE_2 given partenterally to control rats *in vivo* caused an increase in heme oxygenase activity with no change in cytochrome P-450 or NADPH-cytochrome *c* reductase activity. $PGF_{2\alpha}$ administered in the same manner had no significant effect on the microsomal parameters measured. These results suggest that E-type prostaglandins produced by tumor cells may be involved in mediating the induction of hepatic heme oxygenase documented in tumor-bearing animals. However, these results do not provide an explanation for the decrease in hepatic microsomal mixed function oxidation parameters previously documented, and other mechanisms for these alterations in hepatic oxidative microsomal function in tumor-bearing animals must be sought.

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LIBRARY

Librarian — *Donna Chornenki*

The library of the Manitoba Cancer Treatment and Research Foundation continues to increase its holdings. At the end of the 1985 year the total count for bound volumes was 5,124. 3,141 books and 1,983 bound journals. 108 journal subscriptions were received on a continued basis, 14 of which were donated by staff members. This is an increase from the previous year of 123 volumes and 4 subscriptions.

The emphasis in selecting material for the library has been placed on the collection of medical and scientific journals. These journals offer a wide scope of up-to-date information. Index Medicus continued to be the chief source for accessing information. The University of Manitoba Medical Library computer system was used for more complete Medline searching. An I.B.M. PC computer has now been purchased. This will be used for accessing the Medlars System of data files. Once this system is in operation the capabilities of the library increase by the availability of immediate information, increased accuracy, in-depth searching, and greater flexibility in search strategy.

The practice of interlibrary loans continues to increase in the number of requests the Foundation Library made to other libraries. This practice of accessing other library collections has presented the Foundation Library with additional sources of information.

1985 completed the first year in sorting and recataloguing the library collection. The scheduled time span is one more year till this task will be completed. Consequently this will produce a current library system that will be compatible with all other current medical and university libraries.

This year the library benefited from a student work practice program. Library technician students from Red River College spent part of their academic year gaining experience in a one-man medical setting. Through this program the Foundation received 8 weeks of student manpower.

The Library has maintained its recognition of having the majority of oncology journals and resource information housed in one collection within the Province of Manitoba. Owing to the importance of interlibrary loans between libraries, requests continue to increase in numbers for loan of materials and answers to reference questions by both other libraries and the public in general.

The Canadian Cancer Society Patient Services Volunteer Programs at the Manitoba Cancer Treatment and Research Foundation

The Canadian Cancer Society continues to enjoy a close working relationship with the Manitoba Cancer Treatment & Research Foundation in providing services to cancer patients and their families.

The focus of these C.C.S. programs is to offer opportunities for patients to find Comfort, Meaning & Dignity by providing "Hope" and "Help".

"Help" is available to needy cancer patients in meeting transportation, accommodation and other costs.

— Rural patients may be assisted with gas expenses or bus fare incurred in getting to the treatment clinic.

— The cost of accommodation at Lennox Bell Lodge may be met for some. Other cancer related guests receive a 20% discount off their Lodge room.

— Pleasant Volunteer Drivers supply rides to and from the patient's home and the clinic at a nominal fee.

— The Lounge Ladies distribute refreshments to the many waiting areas of the clinic.

— Restored ladies wigs, turbans, and scarves are available free of charge.

— Children's new wigs are funded.

— The clinic's Camp for Children with Cancer is totally funded by the C.C.S.

— Oncology professionals may be assisted with the costs of attending conferences.

"Hope" is offered through Emotional Support Volunteers who have been there".

— Trained Mastectomy Visitors offer encouragement and practical help.

— Trained CanSurmount Visitors assist newly diagnosed patients to cope by visiting informally at the Clinic, or providing one to one visits.

— Jeffrey's Folks offer support to parents of children with cancer.

VOLUNTEERS — 1985

George Ackerman
Ella Adams
Judi Adams
Livvy Aftanas
Kay Ahoff
Ellen Andison
Louise Baker
Paul Bergman
Audrey Bird
Margaret Bonar
Mary Bosman
Tina Bondeson
Mary Brennan
Marjorie Brotheridge
Marion Burwash
Margaret Campbell
Mary Carey
Doris Caufield
Mae Chatfield
Karen Christie
Marjorie Currie
Randy Dalton
Lillian Danish
Thelma Erikson
Noreen Gillanders
Fanny Goldenberg
Murray Greenfield
Norma Haslam
Fred Hayward
Lesli Hermanson
Fay Hoch
Julie Isleifson
John Jack
Becky Joyce
Bonny Kahanovitch
Susan Keller
Barbara King
Ben Kirsh
Florence Kristinson
Emma Lamb
Deanne Lander
Noel Larocque
Madge Letourneau
Alla Lockhart
Anne MacKay
Margaret McLeod
Lorna Marshall
Christa Mason
Fran Mason
Bev. Mathieson
Esther McCubbin
Megan McEnturff
Allisson McKay
Mary Louise McKenzie
Violet McKenzie
Alice McLennan
Kay McNeil
Evelyn Molotsky
Sydney Morgan
Phyllis Nazeravich
Anne Neal
Netta Nicholson
Darlene Nickel
Diane Norman
Ruth Palachuk
Rosemarie Prescitelli
Adair Phelps
Toby Pollock
Shirley Poole
Tarra Pope
Norah Quinton
Dorothy Rankin
Kay Rokala
Susan Romanchuk
Sarah Runions
Inez Salter
Helen Scoble
Ann Shade
Olive Simpson
Margaret Slater
Mona Sorby
Dorothy Sly
May Southam
Jean Stewart
Bernice Syvolos (deceased)
Bernice Taylor
Esther Taylor
Blanche Thompson
Margaret Thompson
Daisy Tooth
Ressa Tod
Helen Vidal
Laurel Walters
Kimberly Weidermann
Myrtle Weir
Lillian Young

These volunteers worked a total of 7,848 hours in 1985.

VOLUNTEER SERVICES ANNUAL REPORT

January — October 1985

prepared by

Judy Searle, Coordinator of Volunteers

As Volunteer Services continued to grow and further establish itself as an integral service in the Cancer Foundation, it held true to its purpose to enhance patient care; to supplement staff in the performance of non-professional duties; to complement their work by providing additional services and comforts to patients and families; to promote good public relations and to ensure a positive growth experience for those assuming the role of volunteer at the Manitoba Cancer Treatment and Research Foundation.

One of the objectives for 1985 was to increase knowledge and rapport amongst volunteers and between the volunteers and the Foundation. A "Volunteer Information Meeting" was a positive measure towards this end. It provided an opportunity for the volunteers, regardless of agency sponsorship and length of volunteer commitment to come together to review the purpose, policies and procedures of Volunteer Services. This was particularly important for those volunteers who had been at the Foundation prior to inception of Volunteer Services (i.e. Canadian Cancer Society Volunteers). They now too became oriented to the role of the volunteers at the Foundation and to the "Policies and Pledge of Confidentiality" (mandatory for all volunteers who enlisted after August, 1983 to read and sign). Furthermore, presented by the Foundation Assistant Director of Nursing (J. Lutz), all volunteers gained further insight into the Foundation and how volunteers fit into its organizational structure in providing service to patients.

The availability of inservices and continuing education for volunteers promotes quality of service by volunteers. Moreover, the Foundation's "investment" in volunteers has a boomerang effect as it in turn increases the volunteers' committment to the Foundation. Volunteer Services will continue to provide such opportunities and ensure whenever applicable the equal availability to volunteers of staff inservices, workshops and the like.

During the year there were a few "inhouse" inservices open to volunteers as well as two major conferences. The Canadian Cancer Society Patient Services Conference was open to all. Many volunteers, both C.C.S. and Volunteer Services recruited, took advantage of this opportunity to acquire more information about the Society and hear the many noted guest speakers. It was a positive learning experience for all who participated.

The Manitoba Health Organization Conference open to all staff and volunteers at no charge attracted a number of volunteers. Of particular interest were the sessions on Volunteer Management and Volunteer Programs, and the presentation by the Manitoba Cancer Foundation Pediatric Oncology Team. This opportunity was greatly appreciated by the conference attendants.

The relationship with the volunteers and staff of the Cancer Society continued to be a positive one. As Coordinator of Volunteers I continued to attend the Patient Services meetings as a non-voting member. All onsite volunteers have developed a cooperative working relationship lending each other assistance whenever necessary.

The CanSurmount Program made great strides in 1985. To date, seven (7) CanSurmount Visitors have been assigned to Chemotherapy and Radiotherapy Clinics, however the number required to meet patient needs must be doubled at minimum. Recruiting potential visitors is primarily the responsibility of C.C.S., but all staff can assist in this endeavour by looking for individuals with potential and informing them of this need. The CanSurmount Program has been positively received by patients and staff. With the skills and enthusiasm of the Foundation's CanSurmount Convenor (G. Ackerman), the program will continue to flourish.

The conjoint volunteer program at the Oncology Unit of the St. Boniface General Hospital has involved five CanSurmount Visitors. The Coordinator of Volunteers, St. Boniface General Hospital continues to be the main liaison with the volunteers. Currently, there is no further need for expansion of volunteer services in that area.

Another annual orientation session for new C.C.S. Volunteer Drivers was successfully held. The drivers became familiar with the Foundation where they transport the majority of their clients. Many thanks go to the Foundation staff who made themselves available for this evening to relay vital information about the clinic and treatment areas.

The Fundraising Coordinator for the Cancer Society called upon the Coordinator and Volunteer Services to arrange a tour of the Foundation as part of their Provincial Fundraising Coordinators Conference. With the great assistance of the Director of Nursing and treatment and clinic area staff a successful event was realized. In addition, several volunteers were trained as tour guides thereby affording them an opportunity to expand their knowledge about the Foundation as well as creating yet another volunteer program.

Recruitment of volunteers by way of radio public service announcement and "word of mouth" (i.e. patient and staff contacts) was required to maintain existing programs as well as meet needs of new programs. As the statistics indicate not only did the volunteer service hours increase in the past year but so did the type and number of volunteer programs. These have included increased or new assignments to Childrens Clinic, Radiotherapy Clinic, CanSurmount, Staff Support (reception), and Special Projects.

Summer was difficult in maintaining volunteer services; basic services, special and urgent requests were met. The staff and patients were most understanding of this summer shortage of volunteers.

As the program stabilized it was necessary to update department resource information and procedures. The "Volunteer Information Handbook" and the Staff and Facility Orientation Guide used during volunteer orientations were revised (the latter by a volunteer). Some Job Descriptions were rewritten to better meet patient and staff needs. Staff and volunteer input were included. A "Policy and Procedure Precis" for Volunteer Services was completed. This precis still requires Administrative approval before accepted as final. A further development involved the use of experienced volunteers in the training of new volunteers. This facilitated the task of staff and provided new volunteers with information directly from "those who know". In addition, it further enhanced the self-esteem of those experienced volunteers involved.

National Volunteer Recognition Week (April 14-20) once again provided an opportunity to

rally staff and volunteer support for volunteer programs as the Foundation and volunteerism in general. As both staff and volunteers have to be thanked for their respective roles in the success of the volunteer programs, representatives of each were treated by Volunteer Services to the Mayor's Awards Luncheon. The distribution of buttons and posters were again well received as was the Photo Display Board illustrating the many volunteer services and the "volunteers in action". The volunteers (on and off site) and staff assembled for the 2nd Annual Strawberry Tea where Certificates of Appreciation were presented to all volunteers and flowers to those who had accumulated 200 or more service hours. This Foundation function was featured in the newspaper "Seniors Today" and the Volunteer Services Photography Album has recorded all of that week's events.

A few highlights of the year has included the continuation of the M.C.F. Newsletter "Herbie's Corner" now published seasonally (four times a year) with ever increasing staff input. The plan for a Patient Information Brochure was revitalized and a final draft has been submitted for administrative scrutiny. The earlier drafts were completed by a volunteer — the latest by a committee of staff members.

A liaison between Volunteer Services and the Transcona Optimist Club which began in December 1984 continued in 1985. With their committment to the Foundation and specifically the children, the club has donated a Digital Blood Pressure Machine to Chemotherapy, funds for a Childrens Corner in Radiotherapy Clinic and a mobile Ice Cream Wagon for all patients to enjoy.

All in all it has been a productive and exciting year. The objectives set forth at the onset of the pilot project for the creation of a position of Coordinator of Volunteers have been realized as the pilot has now officially terminated. The expanded role of volunteers at the Foundation has been welcomed and appreciated. The support of the Administration and Board of the Manitoba Cancer Foundation to continue this program indicates the acceptance of volunteers as a positive and integral component in the health care team of cancer patients. The coming years will prove even more exciting as the programs further grow and develop to meet the ever increasing needs of patients and staff.

VOLUNTEER SERVICES ANNUAL REPORT
November — December, 1985
prepared by
Elaine Hickerson, Co-ordinator of Volunteers

The MCTRF volunteers Christmas Hamper Project was expanded in 1985. 23 families received hampers, two others were given gift packages. The Committee was co-chaired by a volunteer and a staff member. Support came from patients, volunteers and staff. Staff at the St. Boniface Radiotherapy Unit and the Canadian Cancer Society also contributed. Spouses and children of volunteers and staff were recruited to help. All names were submitted to the Christmas Cheer Board. The Transcona Optimist Club and the Manitoba Paramedical Association continued their support. CUPE, Local 500 gave a very generous donation. Safeway Employees Association donated a large carton of new toys. $1158 were collected and $1102 were spent. The $56. balance was added to the $191. balance from 1984. The surplus will be used to assist patients in the coming year.

EPIDEMIOLOGY AND BIOSTATISTICS

DIRECTOR — N. W. Choi, M.D., M.P.H., Ph.D., F.A.C.E.

BIOSTATISTICIANS — N. A. Nelson, B.A., M.A., Ph.D.; P. F. Moodie, B.Sc. Hons., M.Sc.

SECRETARY

M.-P. Regan

RESEARCH FELLOW

A. Ruder, B.A., Ph.D.

FIELD INVESTIGATORS

M. Conway, J. Du, C. Gillon, C. Sobie

DATA PROCESSING

M.-P. Regan

Introduction

The studies that have been conducted in the department range from descriptive and analytical epidemiological studies to evaluation and statistical studies. Studies on interaction of genetics and environmental factors became an added component of our programme in this year. Significant aspects of our research this year have continuously been in the various issues of "iatrogenic diseases" and natural and industrial environment and host factors associated with human cancers.

The following report outlines the progress of the on-going projects and briefly describes the nature of the new studies.

IS NEONATAL VITAMIN K ADMINISTRATION RELATED TO CHILDHOOD CANCER?

N. W. Choi, N. A. Nelson, P. F. Moodie, A. M. Ruder, L. G. Israels

For 30 years vitamin K has been administered to newborns as a prophylactic measure against hypoprothrombinemia or hemorrhagic disease of the newborn. Because of an association of vitamin K with higher tumor incidence and tumor growth acceleration in animal studies, we investigated vitamin K administration to children born in the Province of Manitoba from 1950-74. A case-control study was implemented to ascertain whether the administration of vitamin K was associated with childhood cancers. In this study, the ratio of randomly selected controls to cases was 2:1 (1470 controls: 750 cases).

The criterion for matching controls was being at risk for cancer at the age of the case during the ascertainment period (i.e., a control is at least as old as the case was when the disease was

diagnosed). Examination of material and newborn charts revealed that vitamin K was administered to 20% of newborns in 1950, increasing to 82% by 1974. Preliminary analyses suggest that some risk may be associated with vitamin K use. However, further analyses are now being conducted to evaluate whether the association observed between vitamin K administration and childhood cancer is due to possible confounding variables.

DIFFERENTIAL LONG-TERM (15 YEAR) MORTALITY AMONG BREAST CANCER PATIENTS

A. M. Ruder, N. W. Choi, N. A. Nelson, P. F. Moodie

In 1985 we reviewed case files of patients who had been interviewed in 1971-73 in a case-control study of breast cancer to obtain survival information. Our purpose was to ascertain if any of the interview parameters had an effect on long-term survival. Overall cancer mortality to November 1985 was 41.4% (63 deaths among 152 patients).

In this study population, although positive family history materially increased breast cancer risk (RR, cases vs controls, 2.80), it was not associated with either earlier diagnosis (earlier stage) or reduced survival. To date, stage is the most significant determinant of survival: 47/75 (62.7%) patients whose disease had spread to lymph nodes or beyond at the time of diagnosis died of cancer, compared with 16/77 (20.8%) of patients diagnosed at an earlier stage ($p < 0.005$). Significant ($p < 0.05$) survival (uncontrolled for stage) differentials also were found for ethnic origin, weight at diagnosis, and numbers of pregnancies and live births. Multivariate analyses are now being conducted.

REPRODUCTIVE AND HORMONAL FACTORS IN SURVIVAL OF BREAST CANCER PATIENTS

A. M. Ruder, P. F. Moodie, N. A. Nelson, N. W. Choi

A followup study was initiated to analyse the relation to reproductive and hormonal parameters to breast cancer survival. Records for 145 breast-cancer patients who participated in a 1973-74 study were updated to include survival to the end of 1985. Overall cancer mortality to December 1985 was 37.9% (53 deaths among 140 patients). Results thus far indicate that stage at diagnosis has a significant effect on survival: among patients whose cancer had spread to lymph nodes or beyond at diagnosis, 41/65 (63.1%) had died by December 1985; among patients diagnosed at an earlier stage, only 12/75 (16.0%) had died ($p<0.0005$). In univariate analyses uncontrolled for stage, among the reproductive and hormonal parameters, only menstrual cycle length was significantly associated with survival, with a higher death rate among those with cycles of 29+ days. Other factors affecting survival included ethnic and familial variables: mother's or father's birthplace and having relatives with breast cancer.

EXOGENOUS HORMONE USE AND MORTALITY AMONG BREAST CANCER PATIENTS

A. M. Ruder, N. A. Nelson, P. F. Moodie, N. W. Choi

A mortality study was implemented at the end of 1985, updating an investigation of the role of exogenous hormones in breast cancer for which 279 patients had been interviewed in

1975-78. The object was to ascertain if any interview parameters were predictors of survivorship. Total cancer mortality to December 1985 was 34.7% (92 deaths among 265 patients). Stage was a significant determinant of survival: 59/108 (54.6%) of patients whose disease had spread to lymph nodes or beyond at diagnosis died of cancer vs 33/157 (21.0%) of patients diagnosed at an earlier stage ($p < 0.005$). Survival analyses, controlling for stage, are now being conducted.

PILOT STUDY OF LUNG CANCER AND DOMESTIC ENVIRONMENT

N. W. Choi, N. A. Nelson, P. F. Moodie, J. Du, C. Gillon, M. Conway

In conjunction with the National Cancer Institute of Canada, Manitoba was involved in a pilot case-control study of lung cancer incidence in Winnipeg. This pilot study was undertaken due to the discovery of elevated levels of the radioactive gas radon and its desintegration products in Canadian homes. The decay products of radon known as radon daughters are carcinogenic. This pilot phase of the study is now completed. 100 cases and 100 controls were interviewed and radon measurements taken.

We have now embarked on a definitive independent study and we will be continuing this work during 1986.

We are still using the questionnaire introduced in the pilot study to obtain personal history and occupation of the patient/control and the family working history for the last 25 years. Part of this questionnaire deals with the type of residence the patient/control occupies, building materials used in those homes as well as heating and cooling systems.

SURVEILLANCE OF ENVIRONMENT ASPECTS RELATED TO CANCER IN HUMANS (SEARCH) — EPIDEMIOLOGY STUDY OF DIET AND PANCREATIC CANCER

N. W. Choi, N. A. Nelson, P. F. Moodie, M. Conway in collaboration with the International Agency for Research on Cancer, France.

This is a case-control study involving many centres around the world. Pancreatic carcinoma is relatively common in Western countries including Canada. In this definitive study which followed a pilot study, we have introduced a modified diet and lifestyle questionnaire that permits us to interview proxies.

All centres have now begun case accrual, and interviews conducted to date already place this collaborative study among the largest studies of cancer of the pancreas ever undertaken. Several centres have or now expect to have data on a majority of their cases obtained through proxy interviews due to the fact that this disease is a very fast progressing one, hence quite often patients are too ill to be interviewed. Despite many unforeseen delays, the study is progressing satisfactorily and completion of data collection is expected by the end of 1986.

SURVEILLANCE OF ENVIRONMENT ASPECTS RELATED TO CANCER IN HUMANS (SEARCH) — BRAIN TUMOURS AMONG CHILDREN

N. W. Choi, N. A. Nelson, P. F. Moodie in collaboration with the International Agency for Research on Cancer, France.

This project is part of the SEARCH group of projects involving interested epidemiologists

from around the world. This study has now been funded and we are ready to start work. We will carry out a case-control study using a questionnaire to evaluate the role of certain compounds such as N-Nitroso and classes of exposure which include diet, drinking water, drugs, vitamins, cosmetics, etc. in the etiology of brain tumours in children.

We will explore the relationship between brain tumour incidence and a variety of other personal characteristics and exogenous exposures.

SURVEILLANCE OF ENVIRONMENT ASPECTS RELATED TO CANCER IN HUMANS (SEARCH) — BRAIN TUMOURS AMONG ADULTS

N. W. Choi, N. A. Nelson in collaboration with the International Agency for Research on Cancer, France.

This is another project of the SEARCH group. Very little is known about the etiology of brain tumours in adults. Among the genetic and environmental factors that have been suggested to be causal are exposures to x-rays and vinyl chloride monomers. However, it seems unlikely that these two factors alone could account for a major proportion of brain tumours. Therefore other possible risk factors have to be explored.

To this effect we plan to conduct a case-control study in collaboration with other centres from around the world. At the last meeting of the collaborators, the group drafted a questionnaire to be used in this study. Work is expected to start early 1986.

INTERNATIONAL STUDY ON RADIATION EFFECTS ON SECOND PRIMARY CANCERS

N. W. Choi, N. A. Nelson, P. F. Moodie, W. Wingert, M. Regan in collaboration with the International Agency for Research on Cancer, France.

This multinational collaborative study to investigate if there are increased risks of having second primary cancers among patients with cervical cancer who were treated with radiation is now completed. All the data from the various centres involved are now in final stage of analysis.

THE EFFECT OF CHEMOTHERAPY ON SITES SUCH AS OVARY, TESTIS, AND HODGKIN'S AS IT RELATES TO SECOND PRIMARY CANCER

N. W. Choi, N. A. Nelson in collaboration with the International Agency for Research on Cancer, France.

This is a case-control study to investigate the effect if any of chemotherapy for cancers of the ovary, testis and Hodgkin's disease on subsequent primaries. Of particular interest are lung, bladder and leukemia cancers. The study protocol has been established and the next step is to abstract the information from patient charts. An indept analysis of the effects of chemotherapeutic agents on second primaries will be undertaken.

INTERNATIONAL COLLABORATIVE STUDY ON MALIGNANT MELANOMA

N. W. Choi, J. Ediger, B. Wingert, M. Regan in collaboration with the International Agency for Research on Cancer, France.

This collaborative study was established primarily to investigate true trends of malignant

melanomas. Manitoba has experienced an increasing trend in this type of cancer over the decades.

The Manitoba data has been included with data from other countries participating in this study and a report of findings should be available in 1986.

INTERNATIONAL COLLABORATIVE STUDY ON CHILDHOOD CANCER

N. W. Choi, N. A. Nelson, M. Regan in collaboration with the International Agency for Research on Cancer, France.

Our department is involved in an international study of childhood cancer. This study involves Manitoba cases of cancer between ages of 0-14, from 1950 to 1983.

Final statistical analysis of our data along with data from other centres will begin shortly and we expect results in 1986.

MAPPING OF CANCER INCIDENCE IN MANITOBA BY GEOGRAPHIC LOCALE

N. W. Choi, N. A. Nelson, P. F. Moodie, M. Regan, B. Wingert

This is an on-going project in our department. In the 1984 Annual Report we outlined our findings regarding the 20 census divisions for the time periods 1965-69, 1970-74 and 1975-79.

In 1986, we propose to expand the analysis of 1980-1984 data and to map the city of Winnipeg for the same time periods. We will divide the city according to the old census divisions (20) and we will compare the observed number of cases for all cancer sites taken from our registry to the expected number of cases.

BIOMETRY PROJECTS

P. F. Moodie and N. A. Nelson

In addition to providing statistical consultation for research projects in physics, radiotherapy, radiology and cell biology, computer programs were developed by us on the Prime mini computer and IBM PC-XT micro computer to supplement those available in the release of Statistical Analysis Package currently implemented on Prime. Our objective is to develop new software and interface it with that existing so that virtually all statistical requests will be able to be accommodated on our in-house computers. This is especially advantageous for the statistical analyses of Manitoba Cancer Registry data and avoids the inconvenience of transcribing registry data to magnetic tape to be transported to the University of Manitoba computer centre.

As biomedical data are typically nonnormal, our current research in statistics involves developing procedures that are appropriate for nonnormal distributions. Often, too much emphasis is placed by statisticians on detecting differences between population means, when it is the variation between populations that should be of concern. For example, a treatment protocol may have a beneficial effect on the average but this effect may vary considerably among patients and this variation in patient response should be assessed. Through simulation studies, we are currently investigating these new tests for variability we are developing and are finding that they behave well for different types of data other than the classical normal.

PUBLICATIONS

Boice J. D., Day, N. E., Choi, N. A. et al. "Second cancers following radiation treatment for cervical cancer — an international collaboration between cancer registries". J.N.C.I. **74:** 955-975, 1985.

Harvey, A. C., Moodie, P. F., Nelson, N. A. et al. Computer analysis of a general diagnostic program: Internist (N^2). Computer Appl. in Med. Care. 64-67, 1985.

Moodie, P. F., Craig, D. B. Special Article: Experimental design and statistical analysis. Can. Anaesth. Soc. J. (in press) 1985.

Nelson, N. A., Moodie, P. F. A robust test for homoscedasticity of covariance matrices. Proc. Amer. Statistical Assoc. Las Vega, p. 160. (Abstract), 1985.

Risch, H. A., Jain, M., Choi, N. W. et al. Dietary factors and the incidence of cancer of the stomach. Am. J. Epidemiol. **122:** 947-959, 1985

Ruder, A. M., Lubin, F. et al. Overweight and changes in weight throughout adult life in breast cancer etiology: A case-control study. Am. J. Epidemiol. **122:** 579-588, 1985.

Young, T. K., Choi, N. W. Cancer risks among residents of Manitoba Indian Reserves — 1970-1979. C.M.A.J. **132:** 1269-1273, 1985.

PRESENTATION

Choi, N. W. Current trends in epidemiologic research on cancer. 8th Joint Scientific Congress, Korean Medical Association and Korean Medical Association of America, Seoul, July 1985.

ONCOLOGY RECORDS AND REGISTRY

Director — H. Schipper, B.A.Sc., M.D., F.R.C.P.(C)
Assistant Director, Records & Registry — J. Ediger, (to 31 May 1985)
G. Hanson, (from 01 July 1985).
Assistant Director, Information Services — B. Wingert, (to 01 Nov. 1985)
P. West, (from 21 Jan. 1986).
Secretary — K. Yaremchuk

CENTRAL CANCER REGISTRY

Senior — J. Kostyra
Health Record Technicians — C. Karaz, G. Walsh, J. Walker,
S. Booth, W. Wingert
Clerical Staff — R. Bresch, A. Cookson, C. Johnson, K. Whalen,
R. Zaroda

RECORDS PROCESSING AREA

Senior — C. Cataford
Records Processing Staff — C. MacLean, J. Redden, G. Aquin (LOA),
V. Chagnon (Term), M. Powder (Term)
Interview Clerk — L. McCombe
Receptionist — G. Haufschild
Courier/Mail Services — M. Varkerti

TRANSCRIPTION SERVICES/FILE CONTROL

Senior — E. Tower
Medical Transcriptionists — V. Nordal, D. Meakin, D. Fry, G. Geeves
File Control Clerks — M. Cabral, F. Shilshtut

INFORMATION SERVICES/OUTREACH COMPUTER SYSTEM

Programmer/Analysts — E. Vanderveen, R. Simpson, J. Ediger
Computer Operator — D. Zimmer
U. of M. Computer Science Co-op Students — R. Cuthbert, D. Cassie,
A. Smith, R. Hassman.

ST. BONIFACE UNIT

Senior — L. Soshycki
Health Record Technician — L. Love
Medical Transcriptionists — A. Werbicki, C. Einarson
Records Processing Staff — K. Friesen
File Control Clerk — N. Van Horne
Receptionist — S. Johnson

OUTREACH PROGRAM

Co-ordinator — A. Nemecek
Pharmacist — D. Dickof
Data Manager — G. Charlo
Secretary — B. Cesmystruk

The information resource vested in the Records and Registry Department is essential to the operation of the Foundation. The Department has undergone a major evolution, offering a raised research profile, an expanded computing facility, and a co-ordinating role in the Outreach Program. These three broad areas of activity are described below.

RECORDS & REGISTRY

SCOPE OF SERVICES

Since its inception in 1937, the Records & Registry Department has undergone numerous mutations which have brought it to its present form: a computerized, multifunctional unit whose primary responsibility is health information processing. As such, its current role includes:

Central Cancer Registry

Activities of this unit can be summarized in two broad areas:

1. The provision of an accurate database for health care planning and quality assurance.

2. The provision of a research database for detailed study of malignant disease, (including epidemiological studies, health care delivery analyses and natural history studies).

To this end, the staff of seven Health Record Technicians (including one Senior) and four Clerk Typists engage in the gathering, recording and maintenance of information for all cancer cases in Manitoba.

In the recent past, the staff in the Registry have undertaken a strong and expanding supportive role in assisting researchers.

The integration of the existing cancer registry with the treatment record for those patients treated at the Foundation provides a desirably comprehensive database, whose utilization we actively encourage. In 1985 approximately 90 requests for information were processed by this area, ranging from simple counts of patients with a given diagnosis to audit of records based on multiple criteria. Approximately one half of these requests originated from the Foundation's Epidemiology and Biostatistics Department with which we have a strong liaison.

Registration in 1985 totalled approximately 6,000 new cancer primaries, 3,230 of which were new treatment patients at Manitoba Cancer Foundation.

The Central Cancer Registry is a contributor to the National Cancer Incidence Reporting System and a participating member in the newly formed National Cancer Registries Association.

Records Processing Area

Services provided include: initial information collection and patient documentation, active patient record maintenance and processing, coordination and documentation of diagnostic reports, and chart material distribution.

As well, support services for the Foundation such as patient escort (in coordination with Volunteer Services), reception, switchboard, courier and mail processing are performed by staff in this section. The staffing complement includes one Senior, three Clerk Typists, one Interview Clerk, one Courier and one Receptionist.

Transcription Services/File Control

This area provides transcription service for clinical dictation within the Foundation, and ensures safe and controlled use of health records. On an average, 250 pieces of dictation, comprising 2800 lines, flow daily through our Transcription Unit. As an outpatient facility, "turnaround time" for transcription services is somewhat more urgent than is usually the case in a traditional inpatient environment. The five Transcriptionists (including one Senior) meet this challenge and its ensuing stresses. We look to greater use of current transcription technology to assist in this function.

The section's File Control clerks handle requests for an average of 500 charts daily, predominantly for use in treatment areas. This very active movement of charts emphasizes the importance of our chart location system.

St. Boniface Unit

Our satellite health record unit provides services to our St. Boniface Oncology Department in all the functional areas noted above. The staffing complement consists of one Senior, two Medical Transcriptionists, one Health Record Technician, one File Control Clerk, one Records Processing Clerk and one Receptionist. As the patient load continues to rise in our newer St. Boniface Department, the unit will likely expand accordingly.

YEAR'S ACTIVITIES

With the recruitment of a new Assistant Director of Records & Registry in July 1985, the department entered a phase of reassessment and change. Along with the day-to-day functions of the department, a number of activities received added emphasis:

1. During the years following the merging of active treatment and registry files, each of the identified functional units were left to operate relatively independently. During the last half of 1985, initial steps were undertaken to perform a comprehensive departmental systems review. This included generation of a complete departmental procedure manual, which is currently in its final stages of production. The primary purpose of the systems review is to ensure optimum efficiency.

2. To facilitate the review and development process, weekly meetings were instituted between the Seniors and the Assistant Director. Interdependence of the units was emphasized and a goal-oriented approach was fostered. Formal goals and objectives were established for each unit and the department as a whole. Further development of the management skills of the Seniors group will be supported in the future.

As well, monthly unit staff meetings were introduced to develop and encourage staff participation in departmental decisions, services and problem-solving.

3. Steps were taken to lay the foundation for a comprehensive departmental Quality Assurance program. Workload measurement statistics were developed and initial efforts made to develop quantitative analysis systems. Measures to assess qualitative elements will be forthcoming in the next stage of the Quality Assurance program.

It should be noted that the quality control process has existed as a defined function in the Central Cancer Registry for some time, and has recently advanced in its scope and execution.

4. Saturation of our existing file space necessitated a special project which involved culling

and assigning of records to a status of active or inactive. This enabled relocation of 40% of our chart holdings to supplementary file storage on the MCF premises, thus providing space for our ever-expanding active chart holdings.

5. A department educational needs analysis was undertaken. Staff have been encouraged to upgrade skills and participate in professional organizations. In-house and outside seminars have been utilized. Monthly intradepartmental lectures have been held on cancer-related topics, facilitated by our Director. These have proved immensely beneficial and we hope to expand this program in the coming year.

6. An expansion of the role of the Health Record Technician in research has been launched. Recognizing their unique skills, the Health Record Technicians have been encouraged to recommend and initiate subjects for study based on their intimate perspective of the Registry. In this way, we intend to promote more aggressively the Registry's significant potential for research.

THE FUTURE

The following goals have been targeted for 1986:

1. A complete review of the health record with respect to format and functional factors is planned. A Forms Committee will be encouraged to participate in this process. Other elements which will follow from this assessment are the formation of a records retention policy and a disposal policy as it pertains to sensitive and/or confidential matter.

2. Foundation-specific records documentation standards will be developed, with input from involved parties. Educational seminars will be held to disseminate expertise in this area.

3. Our Health Record Technician staff constitutes a valuable and recognized resource in terms of oncological disease coding. Utilization of this expertise will be encouraged in the health record community. As well, a link between our Registry and the Red River Community College's Health Record Technician Course recognizes and utilizes this expertise.

INFORMATION SERVICES

INTRODUCTION

The major responsibility of Information Services, the computing division of the Records & Registry Department, is support and maintenance of the electronic compliment of our health record holdings. Since 1982, a Prime minicomputer has been the repository of an online, menu-driven medical information management system that is comprised of two major components: a Patient Identification database and a Case Registration database.

The Patient Identification database (184,292 records) contains basic demographic data for all patients treated by the Foundation since 1937. Data recorded includes a central registration number (as well as other hospital and provincial medical registration identifiers used for cross-referencing), patient name (maiden name and/or known alias if applicable), address, dates of birth and death, and Foundation physician.

The Case Registration database (128,245 records), which is linked to the Patient Identification database by the central registration number, contains information about each primary neoplasm. This encompasses data with regard to disease site (international disease code, topography, morphology, metastatic sites, staging information when available); diagnostic

process (date, method, institution); laboratory results; treatment specifics; and if applicable, information related to the death of the patient (date, cause, autopsy results, death registration number).

Extensive data handling features are resident within the information management system, allowing authorized health care professionals the ability to: access patient information with elaborate alphabetic and numeric inquiry techniques; update the contents of existing patient records; edit audit-identified discrepancies in records; and delete records which have been identified as duplicate entries.

Guidelines regulating access to the data, computing personnel and resources of the Foundation are described in the Records and Registry Access Guidelines.

ACTIVITIES

1) *SUPPORT SERVICES:*

Resources, either purchased or developed internally, that allow the creation, maintenance and analysis of databases on the Prime 2550 minicomputer are available to qualified investigators. To date, databases are supported for the following projects:

Vitamin K Study

The Department of Epidemiology and Biostatistics is investigating whether the administration of Vitamin K to Manitoba newborns increases their risks of developing cancer. A data management system was used to input and manipulate over 2000 records, each with 105 variables. Analysis is facilitated through access to the statistical analysis system called "SAS".

Lung Environment Study

The Department of Epidemiology and Biostatistics has extended a study initiated collaboratively with the University of Toronto. A 30-page questionnaire is used to collect information regarding the home and work environments of cancer patients. A control population will also be studied. It is estimated that over 500 questionnaires will be administered.

Quality of Life

A database permitting quality of life analysis of clinical trials outcome, particularly in breast cancer, is accumulating on the Prime minicomputer. Cancer patients self-administer a repeatable, 22-item questionnaire designed to assess factors such as psychosocial state, sociability, and somatic sensation, which may play a role in determining the patient's functional response to the disease and its treatment.

Hairy Cell Leukemia

A database was established to aid investigators in accessing the efficacy of treating hairy-cell leukemia patients with the investigational drug 2'-deoxycoformycin. Data captured includes: patient demographics, previous treatments or therapies, hematology/biochemistry results and chemotherapy toxicity data.

2) *UNIVERSITY OF MANITOBA DEPARTMENT OF COMPUTER SCIENCE COOPERATIVE OPTION PROJECTS:*

Honours Computer Science students enrolled in the Cooperative Option are required to seek employment in a computing workplace for one 4-month period of each university calendar year.

Information Services has initiated a number of projects in association with this program. Student activities are coordinated by Dr. Matthias Laucht, Professor of Computer Science.

Gamma Counter Monitoring System
R. Cuthbert

The data capture and analysis of a Cell Biology Institute gamma counter (LKB WALLAC 1282 Compugamma Universal Gamma Counter) has been automated. The gamma counter communicates directly with the Prime 2550 minicomputer. A video terminal and dot-matrix printer, located at the gamma counter workstation facilitate user interaction with the minicomputer and gamma counter. The minicomputer receives data from predefined gamma counter experiments, interprets it, and generates event logs, summary reports, or error messages with associated recovery procedures.

Immunoprotein Lab Patient File System
R. Hassman, A. Smith

This system is used to manage laboratory test results, providing online data entry, inquiry, update and deletion capabilities. The laboratory typically processes 55 patients with an average of 6 tests per patient. Tests results for as many as 25 different procedures are stored on an IBM PC/AT configured with two 20Mb fixed disks and a single 1.2Mb floppy disk.

Foundation Inventory System
D. Cassie

A database was designed to allow the capture of up-to-date information on the entire equipment inventory housed within the Foundation. For each item there exists a detailed record containing data such as description, location, purchase/replacement cost, and when relevant, service contract pricing. A reporting system allows sorting of the inventory based upon item, department and location.

Resource Usage Accounting System
R. Cuthbert

The Resource Usage Accounting System maintains user and department-specific files regarding the amount of connect, input/output, and central processor time consumed. Each user's resource consumption is further broken down by the time at which the resource was used, and the type of job performed (batch or online). The amount of disk storage used daily by each Cancer Foundation department is also recorded. The system will provide Information Services and the respective departments with a detailed assessment of the amount of computer resource used. This will allow Information Services to project future computing hardware, software and personnel requirements.

3) *OUTREACH:*

The Manitoba Cancer Foundation Outreach Program is highly dependent upon the rapid

accurate storage, transfer and analysis of data. The computer network is being developed to assist in the management of protocols, clinics, laboratories, and the health record.

MINICOMPUTER CONFIGURATION

Hardware:	Prime 2550 processor	
	3 Mb memory	
	300 Mb fixed media disk	
	150 Mb fixed media disk	
	magnetic tape subsystem	
	300 LPM character matrix printer	
	14 video terminals	
Software:	Database management —	INFORMATION
		SIMPLE
		ESCAPE
		MIDASPLUS
	Programming language — COBOL	
	Statistical analysis — SAS	

OUTREACH PROGRAM

The Cancer Foundation Outreach Program is a multi-disciplinary program involving physicians, pharmacy, health records and nursing. It is coordinated through Records and Registry. It began in 1978 as a grant-funded project intended to develop techniques to provide community based cancer treatment to rural Manitobans without compromising either care quality or data acquisition. Brandon, Dauphin, Flin Flon, Thompson and the Pas were the original Outreach centres.

As announced in the Throne Speech of March 1985, Outreach has been adopted as a permanent health care program. Over the next two years, five further rural centres will be established, urban community hospitals in Winnipeg will be integrated into the program and the entire system computerized.

The specific criteria for Outreach Centre selection, physician selection and patient entry are summarized below:

Facility Selection

Those facilities designated as Outreach Centres must meet the following criteria:

- An estimated minimum patient accrual of 25 patients per year per clinic.
- A local medical association able to select two of its membership to assume responsibility for local administration of the program.
- A local hospital which has the physical space available to provide the clinic setting.
- Laboratory facilities able to provide the basic hematology and biochemistry necessary for safe administration of chemotherapeutic agents.
- Pharmacy facilities able to supply chemotherapeutic agents and act as a clinical resource.
- The ability to meet standards of pharmacy, laboratory, nursing and medical care.

Physician Selection

- Two Outreach physicians, preferrably family practitioners, are selected by the local medical association, subject to the approval of the Manitoba Cancer Treatment and Research Foundation.
- They are licensed physicians in good standing, resident in the Outreach area they serve.
- They agree to undertake initial and updating training as required by the Outreach Program.
- They agree to manage individual patients according to treatment plans established by the consulting specialist.
- They agree not to initiate or manage treatment of any individual patient without the consultation and supervision of a specialist oncologist.
- They understand fully their role as community cancer physicians, and in each individual case encourage and maintain the supporting role of the referring community physician.

Patient Selection

A patient is eligible to receive treatment at an Outreach Center subject to the following criteria:

- He/she resides in an Outreach catchment area.
- He/she has treatment planned by a specialist oncologist through the Manitoba Cancer Foundation.
- He/she is under the care of a designated Outreach physician.
- He/she receives treatment and follow-up in the designated Outreach Center by Outreach physicians and nurses.

RECORDS AND REGISTRY ACCESS GUIDELINES

1. Projects must be approved by the Director, with the advice of the Records & Registry Research Advisory Committee according to the following criteria:
   i. The goals of the Cancer Registry.
   ii. The adequacy of research design.
   iii. Personnel, computer & other demands.
   iv. Current operational demand.
2. Projects may be of three types:
   i. *Operational:* Necessary to the day-to-day function of the Manitoba Cancer Treatment and Research Foundation, eg. site reviews, radiotherapy utilization studies, etc. These may be undertaken only by MCF staff in their fields of expertise.
   ii. *Research:* Open to all qualified researchers. Must be approved by the Ethics Committee, U. of M. Any appropriate utilization of the resource is encouraged. In particular natural history, epidemiology and econometric studies are encouraged. Clinical studies may also be reviewed by the Protocol Review Committee of the Foundation.
   iii. *Computer applications:* The computer resource is available to MCF personnel for

analytic, process control and other applications as may be deemed feasible from time to time by the participants.

3. Pilot projects and feasibility studies are encouraged and may be supported by Records & Registry staff as resources permit.
4. All projects must be reviewed by the Records & Registry staff for statistical and computational feasibility *prior* to review by the Director. Applicants should view this process as consultative, intended to minimize effort and maximize utilization of the resource.
5. For all projects, *strict* confidentiality must be assured at all times. All persons accessing the registry will be required to sign an oath of confidentiality.
6. While the primary objective of Records and Registry review is to assure efficient and proper use of the Registry and confidentiality, research proposals which have not been externally funded and/or have not undergone independent peer review, may also be examined as to scientific merit. Clearly projects involving extensive staff and resource commitments will be closely reviewed.
7. All projects will be priorized by the Director. The operational requirements of the registry will always take precedence over research activity and may, from time to time, occupy all available resources. Staff will attempt to schedule research projects so as to minimize such inconveniences to the investigators. Priorization guidelines will include:
   1. Size of staff and computer requirements.
   2. Scientific merit as it relates to the goals of the Registry.
   3. Project deadline.
   4. Funding status of the project.
8. Projects of type (ii) & (iii), Item 2, will be charged for resource utilization at rates to be established from time to time. These charges may include:
   i. Statistical consultation time.
   ii. Programming & programming assistance.
   iii. Computer utilization time.
   iv. Medical records staff time.
   v. Consumables, telephone charges, etc.
9. The data remain the property of the MCF, and users must acknowledge the Registry in publications and presentations.
10. Researchers who require consultation will be encouraged to use the Manitoba Cancer Foundation resource for data analysis to maximize utlization of the experience and expertise of Manitoba Cancer Foundation staff.
11. MCF Records & Registry will assume no responsibility for the accuracy of data reported by investigators using the Registry, or for any interpretations thereof.
12. Researchers must agree to submit to the Director all papers and reports for publication for review prior to distribution or publication to assure that the anonymity of respondents is preserved and that any reference to the Registry is factually correct.

GRANTS FOR RESEARCH AWARDED BY THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION FOR 1985-1986

OPERATING GRANTS

A. Begleiter et al
Studies in Chronic Lymphocytic Leukemia

J. Gerrard et al
Monoclonal Antibodies

N. Kobrinsky
Use of Naloxome for Control of Nausea and Vomiting Associated with Cancer Chemotherapy in Children.

T. Lee et al
Measurement of Regional Cerebral Blood Flow and Xenon Position Coefficient in Patients With Glioblastoma Multiforme

S. Shalev and K. Malaker
Post Film Enhancement by Digital Processing

P. Hahn and S. Shalev
The Application of Risk Analysis to Radiotherapy Treatment Planning.

EQUIPMENT GRANTS

D. Chow
Central 7R Refrigerated Centrifuge

J. Gerrard
FS-1000 Cryosectioning System for MT2B

A. Greenberg
Optomax Image Analyser

F. Paraskevas
NAPCO 6100 C02 Incubator

ONGOING CAREER REWARDS

A. Begleiter
M. Mowat

POSTDOCTORAL FELLOWSHIP

A. Ruder

STUDENTSHIPS

R. Kraut
D. Lowe

AUDITOR'S REPORT TO THE MEMBERS FOR THE YEAR ENDING MARCH 31, 1986

Coopers
&Lybrand

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a member firm of
Coopers & Lybrand (International)

May 31, 1986

AUDITORS' REPORT TO THE MEMBERS

We have examined the balance sheet of The Manitoba Cancer Treatment and Research Foundation as at March 31, 1986 and the statement of revenue and expense and surplus of the general account, the statement of clinical investigation account transactions and the statement of research account transactions for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests and other procedures as we considered necessary in the circumstances.

In our opinion, these financial statements present fairly the financial position of the Foundation as at March 31, 1986 and the results of its operations for the year then ended in accordance with the accounting principles as set out in note 1 to the financial statements, applied on a basis consistent with that of the preceding year.

Coopers & Lybrand

CHARTERED ACCOUNTANTS

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

BALANCE SHEET AS AT MARCH 31, 1986

A S S E T S

	1986 $	1985 $
GENERAL ACCOUNT		
Cash and term deposits	909,968	940,366
Amounts owing by the Manitoba Health Services Commission	140,040	131,992
Amounts owing by the Province of Manitoba	47,500	52,443
Accounts receivable	22,408	33,943
Inventory of supplies - at cost	32,812	40,541
Prepaid expenses	23,980	7,159
Equipment - at nominal value (note 1)	1	1
	1,176,709	1,206,445
CLINICAL INVESTIGATION ACCOUNT		
Cash and term deposits	312,605	289,378
RESEARCH ACCOUNT		
Cash	189,161	60,746
Accounts receivable and accrued interest	237,491	248,362
Investments - Schedule A	4,804,806	4,365,953
	5,231,458	4,675,061

SIGNED ON BEHALF OF THE FOUNDATION

Member

Member

L I A B I L I T I E S

	1986 $	1985 $
Accounts payable and accrued liabilities	554,773	625,993
Term bank loan (note 2)	47,850	76,650
Surplus	574,086	503,802
	1,176,709	1,206,445
Commitments payable	312,605	289,378
Accounts and grants payable	164,540	108,432
Research fund	5,066,918	4,566,629
	5,231,458	4,675,061

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

GENERAL ACCOUNT

STATEMENT OF REVENUE AND EXPENSE AND SURPLUS

FOR THE YEAR ENDED MARCH 31, 1986

	1986 $	1985 $
REVENUE		
Manitoba Health Services Commission	6,949,902	7,026,988
Province of Manitoba	190,000	186,168
Recoveries from other institutions	61,965	61,710
	7,201,867	7,274,866
EXPENSE		
Operating expenses -		
Salaries and benefits	5,427,934	5,145,494
Building occupancy	591,450	612,825
General expenses	343,864	374,521
Supplies and other departmental expenses	237,816	150,761
Diagnostic services	184,745	166,674
	6,785,809	6,450,275
Equipment purchases (note 1)	440,859	805,694
	7,226,668	7,255,969
EXCESS OF REVENUE OVER EXPENSE (EXPENSE OVER REVENUE)	(24,801)	18,897
DEFICIT RECOVERABLE FROM MANITOBA HEALTH SERVICES COMMISSION	24,801	-
	-	18,897
OTHER INCOME - net	70,284	64,275
SURPLUS FOR THE YEAR	70,284	83,172
SURPLUS - BEGINNING OF YEAR	503,802	420,630
SURPLUS - END OF YEAR	574,086	503,802

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

STATEMENT OF CLINICAL INVESTIGATION
ACCOUNT TRANSACTIONS

FOR THE YEAR ENDED MARCH 31, 1986

	1986 $	1985 $
RECEIPTS		
Grants received	836,415	929,161
DISBURSEMENTS		
Breast screening study	242,581	245,918
Researcher and support staff	160,267	165,364
Breast cancer adjuvant studies	46,318	44,345
Outreach program study	44,070	62,937
Physics research and development	43,275	85,932
Lonidamine - hypernephroma	41,672	32,834
Studies of lung cancer	30,711	10,973
Lethal heating of tumour cells feasibility study	30,672	44,692
Physics of light transmission in breast lesion detection	28,820	75,210
Terry Fox career awards	27,121	79,473
Studies on pancreatic cancer	18,195	7,067
Coordinator of volunteer services	12,478	26,891
Bone Imaging Radiopharmaceuticals	10,459	-
Digital Imaging	9,295	-
Methotroxate protocol in treatment of colorectal cancer	4,500	-
World Health Organization "Study of Cancer of Cervix"	1,324	6,086
Other studies	61,430	46,663
Research material	-	20,700
Organ imaging	-	12,712
	813,188	967,397
EXCESS OF RECEIPTS OVER DISBURSEMENTS (DISBURSEMENTS OVER RECEIPTS)	23,227	(38,236)
COMMITMENTS PAYABLE - BEGINNING OF YEAR	289,378	327,614
COMMITMENTS PAYABLE - END OF YEAR	312,605	289,378

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

STATEMENT OF RESEARCH ACCOUNT TRANSACTIONS

FOR THE YEAR ENDED MARCH 31, 1986

	1986			1985
	Unrestricted $	Restricted $	Total $	Total $
REVENUE				
Donations - Schedule B	365,861	63,799	429,660	418,326
Investment income	507,116	4,107	511,223	544,041
	872,977	67,906	940,883	962,367
EXPENSE				
Cell Biology	57,368	51,777	109,145	132,324
Research grants and personnel awards	307,420	-	307,420	273,120
Miscellaneous	24,029	-	24,029	1,942
	388,817	51,777	440,594	407,386
EXCESS OF REVENUE OVER EXPENSES	484,160	16,129	500,289	554,981
FUND BALANCE - BEGINNING OF YEAR	4,339,217	227,412	4,566,629	4,011,648
FUND BALANCE - END OF YEAR	4,823,377	243,541	5,066,918	4,566,629

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

NOTES TO FINANCIAL STATEMENTS

FOR THE YEAR ENDED MARCH 31, 1986

1. SIGNIFICANT ACCOUNTING POLICIES

General Account

Basis of presentation

The financial statements have been prepared in accordance with generally accepted accounting principles except that annual expenditures for equipment acquisitions are charged directly to operations.

Revenue

Revenue received from the Manitoba Health Services Commission for net insured patient costs is based on operating budget amounts approved annually and adjusted for amounts to be returned to or recovered from the commission in respect of surplus or deficit arising in the current fiscal year.

Surplus and deficit

The Foundation is entitled to retain surpluses arising from excess of revenue over approved expenses for each fiscal year up to a maximum of 2% of the net insured patient costs. Any surplus amount in excess of the maximum is returned to the Manitoba Health Services Commission.

The Foundation may recover deficits arising from excess of approved expense over revenue by making application to the Manitoba Health Services Commission.

Clinical Investigation Account

Basis of presentation

The Clinical Investigation Account segregates grants received for specific clinical research projects undertaken by the Foundation. Grants received and disbursements made are recorded on a cash basis. In general, the term of these projects varies from one to three years.

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

NOTES TO FINANCIAL STATEMENTS

FOR THE YEAR ENDED MARCH 31, 1986

1. SIGNIFICANT ACCOUNTING POLICIES (cont'd)

Research Account

Investments

Investments are recorded at cost with any premium or discount being amortized over the term of the investment.

Investment income is recorded on the accrual basis.

Grants

Grants are included in the expenditures of the Research Fund in the year they are approved.

2. TERM BANK LOAN

	1986 $	1985 $
Term bank loan with interest at the bank's prime rate, repayable monthly at $2,400 plus interest, maturing 1987	47,850	76,650

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SCHEDULE A

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

RESEARCH ACCOUNT

SCHEDULE OF INVESTMENTS AS AT MARCH 31, 1986

	Book value $	Market value $
Bonds and debentures -		
B.C. Telephone Company -		
9 7/8%, November 1, 2003	50,000	48,475
Bell Canada -		
11 5/8%, May 2, 1990	257,364	265,875
Government of Canada -		
13%, June 1, 1987	100,000	103,950
13%, June 1, 1987	99,968	103,950
13%, June 1, 1987	99,968	103,950
10 1/2%, March 15, 1988	300,000	307,500
10 1/2%, March 15, 1988	49,871	51,250
12 1/4%, November 1, 1989	100,000	109,500
9 1/4%, May 15, 1997	100,000	101,850
9 1/4%, May 15, 1997	100,000	101,850
Investors Group Debentures -		
9 7/8%, October 4, 1998	50,000	49,225
Ontario Hydro Bonds -		
9 1/2%, February 10, 2000	400,000	398,400
Province of Ontario -		
11 1/4%, March 7, 1989	74,812	78,188
Quebec Hydro -		
17 1/2%, March 16, 1987	205,616	212,088
T. Eaton Acceptance -		
12 1/2%, July 15, 1990	207,214	210,300
Royal Bank of Canada -		
10%, December 1, 1994	160,000	160,880
Credit Foncier -		
16 3/8%, May 10, 1987	15,253	15,000
16%, May 27, 1987	20,303	20,000
16%, June 8, 1987	15,230	15,000
16%, June 22, 1987	15,233	15,000
16%, July 2, 1987	15,235	15,000
13 1/8%, September 10, 1987	25,000	25,000
Carried forward	2,461,067	2,512,231

Coopers &Lybrand

SCHEDULE A
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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

RESEARCH ACCOUNT

SCHEDULE OF INVESTMENTS AS AT MARCH 31, 1986

	Book value $	Market value $
Brought forward	2,461,067	2,512,231
Bonds and debentures (cont'd) -		
Credit Foncier (cont'd) -		
13 1/8%, September 7, 1987	25,000	25,000
13 1/8%, September 7, 1987	25,000	25,000
12 1/2%, October 22, 1987	25,000	25,000
12 1/4%, November 8, 1987	15,000	15,000
12%, January 7, 1988	15,000	15,000
11 3/4%, February 17, 1988	24,867	25,000
Canada Treasury Bills -		
8.4%, April 18, 1986	99,281	101,588
8 1/2%, May 16, 1986	99,591	101,933
Manitoba Pool Elevators -		
11.95%, April 14, 1986	200,000	200,000
	2,989,806	3,045,752
Deposit receipts and investment certificates -		
Bank of Montreal -		
16 1/2%, July 24, 1986	150,000	150,000
Bank of Montreal Mortgage Corporation -		
16%, July 20, 1987	330,000	330,000
12 1/4%, August 3, 1988	300,000	300,000
Canada Trust -		
11 5/8%, August 25, 1986	100,000	100,000
10 1/8%, December 2, 1989	100,000	100,000
Montreal Trust -		
11 7/8%, August 25, 1986	150,000	150,000
11 1/4%, October 2, 1990	20,000	20,000
National Trust -		
11 1/4%, December 17, 1986	200,000	200,000
10 1/8%, December 4, 1989	70,000	70,000
Royal Trust -		
14 3/4%, May 1, 1986	10,000	10,000
16 7/8%, June 21, 1987	225,000	225,000
11 1/8%, December 18, 1988	10,000	10,000
10 1/4%, December 19, 1990	150,000	150,000
	1,815,000	1,815,000
	4,804,806	4,860,752

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SCHEDULE B

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

SCHEDULE OF RESEARCH RECEIPTS

FOR THE YEAR ENDED MARCH 31, 1986

	$
UNRESTRICTED DONATIONS	
In memory of Albert Allen	658
In memory of Mr. Otto Anderson	385
Donation Bike-a-thon	10,419
Estate A. Billinkoff	500
In memory of Theodore Bishop	300
In memory of Dr. G. Frank Boult	350
In memory of Bruce Brown	1,575
In memory of John L. Brownstein	400
In memory of Shirley Charge	600
In memory of Mr. Kozimar S. Chopp	400
Donation Controlled Environments Ltd.	400
Donation G. R. Collyer	1,000
In memory of Dr. J. Crust	1,512
Donation Hazel Cumpstone	1,000
In memory of Gladys F. Couch	500
In memory of Edwin Danish	300
In memory of Mrs. Bonnie Davies	303
Estate Muriel Davies	3,000
Estate Kathleen Edward	4,167
Donation Elizabeth Evans	450
In memory of Mrs. A. Folger	340
Donations Steve Fonyo Run	00
Estate K. T. Froning	15,000
Estate M.G. Gauthier	8,150
Estate Sadie B. Gillies	2,000
In memory of John J. Goring	514
Donation Miss E. Grierson	1,700
In memory of Mrs. Georgina Guth	505
Estate Gertrude E. Hay	24,208
Donation Health Sciences Centre Charitable Fund - Employees	3,725
In memory of Colin N. Hector	881
Donation Mr. & Mrs. A. Heide	500
Donation Lisa Hogg	500
Donation Dr. Donalda A. Huggins	500
Donation Imperial Veterans in Canada Branch #84	300
Estate Bertram M. Jones	303
Estate R. T. Jordan	2,000
In memory of Morris Katz	5,865
Estate E. Komarchuk	5,000
In memory of Mr. Charles Kroft	3,000
Estate Miss Irene Lesiuk	2,000
Donation Mrs. H. Lucas	1,000
In memory of Mr. D. MacDonald	533
Donation Esther Maizlen	400
Carried forward	107,543

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SCHEDULE B
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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

SCHEDULE OF RESEARCH RECEIPTS

FOR THE YEAR ENDED MARCH 31, 1986

	$
UNRESTRICTED DONATIONS (cont'd)	
Brought forward	107,543
Donation Dr. A. S. Majury	500
Donation Manitoba Hydro Selkirk Employees Charitable Donations Fund	1,000
Donation Mary McKenty	1,000
Estate Florence McKeown	500
Donation Miss E. Mitchell	350
Estate Winifred I. Northcott	1,000
Donation Nick Osesky	500
In memory of Mr. Edward W. Packolek	510
In memory of Norman Patrick	525
In memory of Roberta Poole	849
In memory of: James Fraser Rea, Elizabeth Ann Rea, Clifford Bryce Rea, Joyce Lillian Rea, Phyllis M. Rea	100,000
Donation Ms. Ngaw Saw-Ying	300
Estate Benjamin Schwartz	500
Estate Miss Kathleen Shaw	22,400
In memory of Mrs. Gwen Smith	905
Estate Hon. J. R. Solomon	1,000
In memory of Hon. J. R. Solomon	325
Donation Standard Aero Ltd. Employees Charitable Donation Fund	1,000
In memory of Timothy F. Sternat	435
Estate Edward H. Stremel	4,000
In memory of Mr. Albert Stuart	867
In memory of Sandra D. Tacchi	430
In memory of Mrs. Kay Tazumi	410
Estate Mrs. Jeannette Thompson	500
Donation Hon. G.E. Tritschler	1,000
Estate Janet Turley	1,000
Donation Mr. Oscar Van deWiebe	1,000
Estate Jessie P. Watson	42,202
In memory of Mr. Max Weinstein	433
In memory of Mr. Wm. Willis	1,225
Carried forward	294,209

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SCHEDULE B
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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

SCHEDULE OF RESEARCH RECEIPTS

FOR THE YEAR ENDED MARCH 31, 1986

	$
UNRESTRICTED DONATIONS (cont'd)	
Brought forward	294,209
Winnipeg Foundation -	
In memory of Samuel & Essie Badham	
Leon A. Brown Ltd.	2,300
Estate Claire M. Gauthier	705
George Gordon Fund	429
Harry Little Family Fund	742
Estate Thomas William & Anna	750
Ronald Lowe Memorial Fund	
Donation Lewis & Pearl C. Roth	2,079
Mr. & Mrs. Joseph Secter	5,804
Donation Samuel & Sally Stern & Son Ronald	1,243
Frank Topper & Emma Topper Memorial Fund	1,017
Bequest Joseph P. Wolinsky	2,583
Estate Victor Zekier	450
In memory of Thelma Young	1,000
In memory of Mr. Joseph Zak	440
In memory of Mr. Walter Zalusky	976
Other memorial contributions and donations in amounts of less than $300	342
	50,792
	365,861

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SCHEDULE B
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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

SCHEDULE OF RESEARCH RECEIPTS

FOR THE YEAR ENDED MARCH 31, 1986

	$
RESTRICTED DONATIONS	
In memory of Mrs. Alice Christie	1,000
David M. Copp Memorial Fund	16,800
Hilde Kaarsoo	500
Ms. Helen Kane	1,000
Kiwanis Club of St. James	500
Kiwanis Club of Winnipeg	10,000
Masonic Foundation of Manitoba	16,964
Russell Noble	500
Pinawa Newstand	500
Mrs. C. Rosenberg	1,000
Gwen & Joseph Secter	5,000
University of Manitoba	8,480
Joseph Wolinsky Foundation	1,000
Other memorial contributions and donations in amounts of less than $300	555
	63,799

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